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PATENT APPLICATION
NOVEL METHODS OF DIAGNOSIS OF ANGIOGENESIS, COMPOSITIONS AND METHODS OF SCREENING FOR ANGIOGENESIS MODULATORS

Inventor(s):

Richard Murray, a citizen of the United States residing at 22643 Woodridge Court, Cupertino, California 95014

Richard Glynne, a citizen of the United Kingdom residing at 2039 Alma Street, Palo Alto, CA 94301

Susan R. Watson, a citizen of the United Kingdom residing at 805 Balra Drive, El Cerrito, CA 94530

Assignee:

EOS Biotechnology, Inc.

Entity: Small

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: 415-576-0200

NOVEL METHODS OF DIAGNOSIS OF ANGIOGENESIS, COMPOSITIONS AND METHODS OF SCREENING FOR ANGIOGENESIS MODULATORS

CROSS-REFERENCES TO RELATED APPLICATIONS

The present application is a continuation-in-part (CIP) of co-pending United States Patent Application "Novel Methods Of Diagnosis Of Angiogenesis, Compositions And Methods Of Screening For Angiogenesis Modulators", Attorney Docket No. A65110-1, filed on August 11, 2000, which claims the benefit of priority to U.S.S.N. 60/148,425 filed August 11, 1999, both of which are incorporated herein by reference.

FIELD OF THE INVENTION

The invention relates to the identification of nucleic acid and protein expression profiles and nucleic acids, products, and antibodies thereto that are involved in angiogenesis; and to the use of such expression profiles and compositions in diagnosis and therapy of angiogenesis. The invention further relates to methods for identifying and using agents and/or targets that modulate angiogenesis.

BACKGROUND OF THE INVENTION

Both vasculogenesis, the development of an interactive vascular system comprising arteries and veins, and angiogenesis, the generation of new blood vessels, play a role in embryonic development. In contrast, angiogenesis is limited in a normal adult to the placenta, ovary, endometrium and sites of wound healing. However, angiogenesis, or its absence, plays an important role in the maintenance of a variety of pathological states. Some of these states are characterized by neovascularization, *e.g.*, cancer, diabetic retinopathy, glaucoma, and age related macular degeneration. Others, *e.g.*, stroke, infertility, heart disease, ulcers, and scleroderma, are diseases of angiogenic insufficiency.

Angiogenesis has a number of stages (see, *e.g.*, Folkman, *J.Natl Cancer Inst.* 82.4-6, 1990; Firestein, *J Clin Invest.*103:3-4, 1999; Koch, *Arthritis Rheum.*41:951-62, 1998; Carter, *Oncologist* 5(Suppl 1):51-4, 2000; Browder *et al.*, *Cancer Res.* 60:1878-86, 2000; and Zhu and Witte, *Invest New Drugs* 17:195-212, 1999). The early stages of angiogenesis include endothelial cell protease production, migration of cells, and proliferation. The early

stages also appear to require some growth factors, with VEGF, TGF-α, angiostatin, and selected chemokines all putatively playing a role. Later stages of angiogenesis include population of the vessels with mural cells (pericytes or smooth muscle cells), basement membrane production, and the induction of vessel bed specializations. The final stages of vessel formation include what is known as "remodeling", wherein a forming vasculature becomes a stable, mature vessel bed. Thus, the process is highly dynamic, often requiring coordinated spatial and temporal waves of gene expression.

Conversely, the complex process may be subject to disruption by interfering with one or more critical steps. Thus, the lack of understanding of the dynamics of angiogenesis prevents therapeutic intervention in serious diseases such as those indicated. It is an object of the invention to provide methods that can be used to screen compounds for the ability to modulate angiogenesis. Additionally, it is an object to provide molecular targets for therapeutic intervention in disease states which either have an undesirable excess or a deficit in angiogenesis. The present invention provides solutions to both.

SUMMARY OF THE INVENTION

The present invention provides compositions and methods for detecting or modulating angiogenesis associated sequences.

In one aspect, the invention provides a method of detecting an angiogenesis-associated transcript in a cell in a patient, the method comprising contacting a biological sample from the patient with a polynucleotide that selectively hybridized to a sequence at least 80% identical to a sequence as shown in Table 1. In one embodiment, the biological sample is a tissue sample. In another embodiment, the biological sample comprises isolated nucleic acids, which are often mRNA.

In another embodiment, the method further comprises the step of amplifying nucleic acids before the step of contacting the biological sample with the polynucleotide. Often, the polynucleotide comprises a sequence as shown in Table 1. The polynucleotide can be labeled, for example, with a fluorescent label and can be immobilized on a solid surface.

In other embodiments the patient is undergoing a therapeutic regimen to treat a disease associated with angiogenesis or the patient is suspected of having an angiogenesis-associated disorder.

In another aspect, the invention comprises an isolated nucleic acid molecule consisting of a polynucleotide sequence as shown in Table 1. The nucleic acid molecule can be labeled, for example, with a fluorescent label,

In other aspects, the invention provides an expression vector comprising an isolated nucleic acid molecule consisting of a polynucleotide sequence as shown in Table 1 or a host cell comprising the expression vector.

In another embodiment, the isolated nucleic acid molecule encodes a polypeptide having an amino acid sequence as shown in Table 2.

In another aspect, the invention provides an isolated polypeptide which is encoded by a nucleic acid molecule having polynucleotide sequence as shown in Table 1. In one embodiment, the isolated polypeptide has an amino acid sequence as shown in Table 2.

In another embodiment, the invention provides an antibody that specifically binds a polypeptide that has an amino acid sequence as shown in Table 2. The antibody can be conjugated to an effector component such as a fluorescent label, a toxin, or a radioisotope. In some embodiments, the antibody is an antibody fragment or a humanized antibody.

In another aspect, the invention provides a method of detecting a cell undergoing angiogenesis in a biological sample from a patient, the method comprising contacting the biological sample with an antibody that specifically binds to a polypeptide that has an amino acid sequence as shown in Table 2. In some embodiment, the antibody is further conjugated to an effector component, for example, a fluorescent label.

In another embodiment, the invention provides a method of detecting antibodies specific to angiogenesis in a patient, the method comprising contacting a biological sample from the patient with a polypeptide comprising a sequence as shown in Table 2.

The invention also provides a method of identifying a compound that modulates the activity of an angiogenesis-associated polypeptide, the method comprising the steps of: (i) contacting the compound with a polypeptide that comprises at least 80% identity to an amino acid sequence as shown in Table 2; and (ii) detecting an increase or a decrease in the activity of the polypeptide. In one embodiment, the polypeptide has an amino acid sequence as shown in Table 2. In another embodiment, the polypeptide is expressed in a cell.

The invention also provides a method of identifying a compound that modulates angiogenesis, the method comprising steps of: (i) contacting the compound with a cell undergoing angiogenesis; and (ii) detecting an increase or a decrease in the expression of a polypeptide sequence as shown in Table 2. In one embodiment, the detecting step comprises hybridizing a nucleic acid sample from the cell with a polynucleotide that selectively hybridizes to a sequence at least 80% identical to a sequence as shown in Table 1.

In another embodiment, the method further comprises detecting an increase or decrease in the expression of a second sequence as shown in Table 2.

In another embodiment, the invention provides a method of inhibiting angiogenesis in a cell that expresses a polypeptide at least 80% identical to a sequence as shown in Table 2, the method comprising the step of contacting the cell with a therapeutically effective amount of an inhibitor of the polypeptide. In one embodiment, the polypeptide has an amino acid sequence shown in Table 2. In another embodiment, the inhibitor is an antibody.

In other embodiments, the invention provides a method of activating angiogenesis in a cell that expresses a polypeptide at least 80% identical to a sequence as shown in Table 2, the method comprising the step of contacting the cell with a therapeutically effective amount of an activator of the polypeptide. In one embodiment, the polypeptide has an amino acid sequence shown in Table 2.

Other aspects of the invention will become apparent to the skilled artisan by the following description of the invention.

Table 1 provides nucleotide sequence of genes that exhibit changes in expression levels as a function of time in tissue undergoing angiogenesis compared to tissue that is not.

Table 2 provides polypeptide sequence of proteins that exhibit changes in expression levels as a function of time in tissue undergoing angiogenesis compared to tissue that is not.

DESCRIPTION OF THE SPECIFIC EMBODIMENTS

In accordance with the objects outlined above, the present invention provides novel methods for diagnosis and treatment of disorders associated with angiogenesis (sometimes referred to herein as angiogenesis disorders or AD), as well as methods for screening for compositions which modulate angiogenesis. By "disorder associated with angiogenesis" or "disease associated with angiogenesis" herein is meant a disease state which is marked by either an excess or a deficit of vessel development. Angiogenesis disorders asociated with increased angiogenesis include, but are not limited to, cancer and proliferative diabetic retinopathy. Pathological states for which it may be desirable to increase angiogenesis include stroke, heart disease, infertility, ulcers, and scleradoma. Also provided are methods for treating AD.

Definitions

The term "angiogenesis protein" or "angiogenesis polynucleotide" refers to nucleic acid and polypeptide polymorphic variants, alleles, mutants, and interspecies homologs that: (1) have an amino acid sequence that has greater than about 60% amino acid sequence identity, 65%, 70%, 75%, 80%, 85%, 90%, preferably 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or greater amino acid sequence identity, preferably over a region of over a region of at least about 25, 50, 100, 200, 500, 1000, or more amino acids, to an angiogenesis protein sequence of Table 2; (2) bind to antibodies, *e.g.*, polyclonal antibodies, raised against an immunogen comprising an amino acid sequence of Table 2, and conservatively modified variants thereof; (3) specifically hybridize under stringent hybridization conditions to an anti-sense strand corresponding to a nucleic acid sequence of Table 1 and conservatively modified variants thereof; (4) have a nucleic acid sequence that has greater than about 95%, preferably greater than about 96%, 97%, 98%, 99%, or higher nucleotide sequence identity, preferably over a region of at least about 25, 50, 100, 200, 500, 1000, or more nucleotides, to a sense sequence corresponding to one set out in Table 1. A polynucleotide or polypeptide sequence is typically from a mammal including, but not limited to, primate, *e.g.*, human; rodent, *e.g.*, rat, mouse, hamster; cow, pig, horse, sheep, or any mammal. An "angiogenesis polypeptide" and an "angiogenesis polynucleotide," include both naturally occurring or recombinant.

A "full length" angiogenesis protein or nucleic acid refers to an agiogenesis polypeptide or polynucleotide sequence, or a variant thereof, that contains all of the elements normally contained in one or more naturally occurring, wild type angiogenesis polynucleotide or polypeptide sequences. The "full length" may be prior to, or after, various stages of post-translation processing.

"Biological sample" as used herein is a sample of biological tissue or fluid that contains nucleic acids or polypeptides, *e.g.*, of an angiogenic protein. Such samples include, but are not limited to, tissue isolated from primates, *e.g.*, humans, or rodents, *e.g.*, mice, and rats. Biological samples may also include sections of tissues such as biopsy and autopsy samples, and frozen sections taken for histologic purposes. A biological sample is typically obtained from a eukaryotic organism, most preferably a mammal such as a primate *e.g.*, chimpanzee or human; cow; dog; cat; a rodent, *e.g.*, guinea pig, rat, mouse; rabbit; or a bird; reptile; or fish.

"Providing a biological sample" means to obtain a biological sample for use in methods described in this invention. Most often, this will be done by removing a sample of

cells from an animal, but can also be accomplished by using previously isolated cells (*e.g.*, isolated by another person, at another time, and/or for another purpose), or by performing the methods of the invention *in vivo*. Archival tissues, having treatment or outcome histroy, will be particularly useful.

The terms "identical" or percent "identity," in the context of two or more nucleic acids or polypeptide sequences, refer to two or more sequences or subsequences that are the same or have a specified percentage of amino acid residues or nucleotides that are the same (i.e., about 70% identity, preferably 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or higher identity over a specified region (e.g., SEQ ID NOS:1-4), when compared and aligned for maximum correspondence over a comparison window or designated region) as measured using a BLAST or BLAST 2.0 sequence comparison algorithms with default parameters described below, or by manual alignment and visual inspection (see, *e.g.*, NCBI web site http://www.ncbi.nlm.nih.gov/BLAST/ or the like). Such sequences are then said to be "substantially identical." This definition also refers to, or may be applied to, the compliment of a test sequence. The definition also includes sequences that have deletions and/or additions, as well as those that have substitutions. As described below, the preferred algorithms can account for gaps and the like. Preferably, identity exists over a region that is at least about 25 amino acids or nucleotides in length, or more preferably over a region that is 50-100 amino acids or nucleotides in length.

For sequence comparison, typically one sequence acts as a reference sequence, to which test sequences are compared. When using a sequence comparison algorithm, test and reference sequences are entered into a computer, subsequence coordinates are designated, if necessary, and sequence algorithm program parameters are designated. Preferably, default program parameters can be used, or alternative parameters can be designated. The sequence comparison algorithm then calculates the percent sequence identities for the test sequences relative to the reference sequence, based on the program parameters.

A "comparison window", as used herein, includes reference to a segment of any one of the number of contiguous positions selected from the group consisting of from 20 to 600, usually about 50 to about 200, more usually about 100 to about 150 in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned. Methods of alignment of sequences for comparison are well-known in the art. Optimal alignment of sequences for comparison. can be conducted, e.g., by the local homology algorithm of Smith & Waterman, *Adv. Appl. Math.* 2:482 (1981), by the homology alignment algorithm of Needleman & Wunsch, *J. Mol.*

Biol. 48:443 (1970), by the search for similarity method of Pearson & Lipman, *Proc. Nat'l. Acad. Sci. USA* 85:2444 (1988), by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, 575 Science Dr., Madison, WI), or by manual alignment and visual inspection (*see, e.g., Current Protocols in Molecular Biology* (Ausubel *et al.*, eds. 1995 supplement)).

A preferred example of algorithm that is suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul *et al., Nuc. Acids Res.* 25:3389-3402 (1977) and Altschul *et al., J. Mol. Biol.* 215:403-410 (1990), respectively. BLAST and BLAST 2.0 are used, with the parameters described herein, to determine percent sequence identity for the nucleic acids and proteins of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (http://www.ncbi.nlm.nih.gov/). This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length W in the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul *et al., supra*). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Cumulative scores are calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always > 0) and N (penalty score for mismatching residues; always < 0). For amino acid sequences, a scoring matrix is used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, an expectation (E) of 10, M=5, N=-4 and a comparison of both strands. For amino acid sequences, the BLASTP program uses as defaults a wordlength of 3, and expectation (E) of 10, and the BLOSUM62 scoring matrix (*see* Henikoff & Henikoff, *Proc. Natl. Acad. Sci. USA* 89:10915 (1989)) alignments (B) of 50, expectation (E) of 10, M=5, N=-4, and a comparison of both strands.

The BLAST algorithm also performs a statistical analysis of the similarity between two sequences (*see, e.g.*, Karlin & Altschul, *Proc. Nat'l. Acad. Sci. USA* 90:5873-5787 (1993)). One measure of similarity provided by the BLAST algorithm is the smallest sum probability (P(N)), which provides an indication of the probability by which a match between two nucleotide or amino acid sequences would occur by chance. For example, a nucleic acid is considered similar to a reference sequence if the smallest sum probability in a comparison of the test nucleic acid to the reference nucleic acid is less than about 0.2, more preferably less than about 0.01, and most preferably less than about 0.001.

An indication that two nucleic acid sequences or polypeptides are substantially identical is that the polypeptide encoded by the first nucleic acid is immunologically cross reactive with the antibodies raised against the polypeptide encoded by the second nucleic acid, as described below. Thus, a polypeptide is typically substantially identical to a second polypeptide, for example, where the two peptides differ only by conservative substitutions. Another indication that two nucleic acid sequences are substantially identical is that the two molecules or their complements hybridize to each other under stringent conditions, as described below. Yet another indication that two nucleic acid sequences are substantially identical is that the same primers can be used to amplify the sequences.

A "host cell" is a naturally occurring cell or a transformed cell that contains an expression vector and supports the replication or expression of the expression vector. Host cells may be cultured cells, explants, cells *in vivo*, and the like. Host cells may be prokaryotic cells such as *E. coli*, or eukaryotic cells such as yeast, insect, amphibian, or mammalian cells such as CHO, HeLa, and the like (see, *e.g.*, the American Type Culture Collection catalog or web site, www.atcc.org).

The terms "polypeptide," "peptide" and "protein" are used interchangeably herein to refer to a polymer of amino acid residues. The terms apply to amino acid polymers in which one or more amino acid residue is an artificial chemical mimetic of a corresponding naturally occurring amino acid, as well as to naturally occurring amino acid polymers and non-naturally occurring amino acid polymer.

The term "amino acid" refers to naturally occurring and synthetic amino acids, as well as amino acid analogs and amino acid mimetics that function in a manner similar to the naturally occurring amino acids. Naturally occurring amino acids are those encoded by the genetic code, as well as those amino acids that are later modified, e.g., hydroxyproline, γ-carboxyglutamate, and O-phosphoserine. Amino acid analogs refers to compounds that have the same basic chemical structure as a naturally occurring amino acid, i.e., an α carbon that is

bound to a hydrogen, a carboxyl group, an amino group, and an R group, e.g., homoserine, norleucine, methionine sulfoxide, methionine methyl sulfonium. Such analogs have modified R groups (e.g., norleucine) or modified peptide backbones, but retain the same basic chemical structure as a naturally occurring amino acid. Amino acid mimetics refers to chemical compounds that have a structure that is different from the general chemical structure of an amino acid, but that functions in a manner similar to a naturally occurring amino acid.

Amino acids may be referred to herein by either their commonly known three letter symbols or by the one-letter symbols recommended by the IUPAC-IUB Biochemical Nomenclature Commission. Nucleotides, likewise, may be referred to by their commonly accepted single-letter codes.

"Conservatively modified variants" applies to both amino acid and nucleic acid sequences. With respect to particular nucleic acid sequences, conservatively modified variants refers to those nucleic acids which encode identical or essentially identical amino acid sequences, or where the nucleic acid does not encode an amino acid sequence, to essentially identical sequences. Because of the degeneracy of the genetic code, a large number of functionally identical nucleic acids encode any given protein. For instance, the codons GCA, GCC, GCG and GCU all encode the amino acid alanine. Thus, at every position where an alanine is specified by a codon, the codon can be altered to any of the corresponding codons described without altering the encoded polypeptide. Such nucleic acid variations are "silent variations," which are one species of conservatively modified variations. Every nucleic acid sequence herein which encodes a polypeptide also describes every possible silent variation of the nucleic acid. One of skill will recognize that each codon in a nucleic acid (except AUG, which is ordinarily the only codon for methionine, and TGG, which is ordinarily the only codon for tryptophan) can be modified to yield a functionally identical molecule. Accordingly, each silent variation of a nucleic acid which encodes a polypeptide is implicit in each described sequence with respect to the expression product, but not with respect to actual probe sequences.

As to amino acid sequences, one of skill will recognize that individual substitutions, deletions or additions to a nucleic acid, peptide, polypeptide, or protein sequence which alters, adds or deletes a single amino acid or a small percentage of amino acids in the encoded sequence is a "conservatively modified variant" where the alteration results in the substitution of an amino acid with a chemically similar amino acid. Conservative substitution tables providing functionally similar amino acids are well known in

the art. Such conservatively modified variants are in addition to and do not exclude polymorphic variants, interspecies homologs, and alleles of the invention.

The following eight groups each contain amino acids that are conservative substitutions for one another:1) Alanine (A), Glycine (G); 2) Aspartic acid (D), Glutamic acid (E); 3) Asparagine (N), Glutamine (Q); 4) Arginine (R), Lysine (K); 5) Isoleucine (I), Leucine (L), Methionine (M), Valine (V); 6) Phenylalanine (F), Tyrosine (Y), Tryptophan (W); 7) Serine (S), Threonine (T); and 8) Cysteine (C), Methionine (M) (*see, e.g.*, Creighton, *Proteins* (1984)).

Macromolecular structures such as polypeptide structures can be described in terms of various levels of organization. For a general discussion of this organization, *see, e.g.*, Alberts *et al.*, *Molecular Biology of the Cell* (3rd ed., 1994) and Cantor and Schimmel, *Biophysical Chemistry Part I: The Conformation of Biological Macromolecules* (1980). "Primary structure" refers to the amino acid sequence of a particular peptide. "Secondary structure" refers to locally ordered, three dimensional structures within a polypeptide. These structures are commonly known as domains. Domains are portions of a polypeptide that form a compact unit of the polypeptide and are typically 25 to approximately 500 amino acids long. Typical domains are made up of sections of lesser organization such as stretches of β-sheet and α-helices. "Tertiary structure" refers to the complete three dimensional structure of a polypeptide monomer. "Quaternary structure" refers to the three dimensional structure formed, usually by the noncovalent association of independent tertiary units. Anisotropic terms are also known as energy terms.

A "label" or a "detectable moiety" is a composition detectable by spectroscopic, photochemical, biochemical, immunochemical, chemical, or other physical means. For example, useful labels include ^{32}P, fluorescent dyes, electron-dense reagents, enzymes (*e.g.*, as commonly used in an ELISA), biotin, digoxigenin, or haptens and proteins which can be made detectable, *e.g.*, by incorporating a radiolabel into the peptide or used to detect antibodies specifically reactive with the peptide.

An "effector" or "effector moiety" or "effector component" is a molecule that is bound (or linked, or conjugated), either covalently, through a linker or a chemical bond, or noncovalently, through ionic, van der Waals, electrostatic, or hydrogen bonds, to an antibody. The "effector" can be a variety of molecules including, for example, detection moieties including radioactive compounds, fluroescent compounds, an enzyme or substrate, tags such

as epitope tags, a toxin; a chemotherapeutic agent; a lipase; an antibiotic; or a radioisotope emitting "hard" *e.g.*, beta radiation.

A "labeled nucleic acid probe or oligonucleotide" is one that is bound, either covalently, through a linker or a chemical bond, or noncovalently, through ionic, van der Waals, electrostatic, or hydrogen bonds to a label such that the presence of the probe may be detected by detecting the presence of the label bound to the probe. Alternatively, method using high affinity interactions may achieve the same results where one of a pair of binding partners binds to the other, *e.g.*, biotin, streptavidin.

As used herein a "nucleic acid probe or oligonucleotide" is defined as a nucleic acid capable of binding to a target nucleic acid of complementary sequence through one or more types of chemical bonds, usually through complementary base pairing, usually through hydrogen bond formation. As used herein, a probe may include natural (*i.e.*, A, G, C, or T) or modified bases (7-deazaguanosine, inosine, etc.). In addition, the bases in a probe may be joined by a linkage other than a phosphodiester bond, so long as it does not interfere with hybridization. Thus, for example, probes may be peptide nucleic acids in which the constituent bases are joined by peptide bonds rather than phosphodiester linkages. It will be understood by one of skill in the art that probes may bind target sequences lacking complete complementarity with the probe sequence depending upon the stringency of the hybridization conditions. The probes are preferably directly labeled as with isotopes, chromophores, lumiphores, chromogens, or indirectly labeled such as with biotin to which a streptavidin complex may later bind. By assaying for the presence or absence of the probe, one can detect the presence or absence of the select sequence or subsequence.

The term "recombinant" when used with reference, *e.g.*, to a cell, or nucleic acid, protein, or vector, indicates that the cell, nucleic acid, protein or vector, has been modified by the introduction of a heterologous nucleic acid or protein or the alteration of a native nucleic acid or protein, or that the cell is derived from a cell so modified. Thus, for example, recombinant cells express genes that are not found within the native (non-recombinant) form of the cell or express native genes that are otherwise abnormally expressed, under expressed or not expressed at all.

The term "heterologous" when used with reference to portions of a nucleic acid indicates that the nucleic acid comprises two or more subsequences that are not found in the same relationship to each other in nature. For instance, the nucleic acid is typically recombinantly produced, having two or more sequences from unrelated genes arranged to make a new functional nucleic acid, *e.g.*, a promoter from one source and a coding region

from another source. Similarly, a heterologous protein indicates that the protein comprises two or more subsequences that are not found in the same relationship to each other in nature (*e.g.*, a fusion protein).

A "promoter" is defined as an array of nucleic acid control sequences that direct transcription of a nucleic acid. As used herein, a promoter includes necessary nucleic acid sequences near the start site of transcription, such as, in the case of a polymerase II type promoter, a TATA element. A promoter also optionally includes distal enhancer or repressor elements, which can be located as much as several thousand base pairs from the start site of transcription. A "constitutive" promoter is a promoter that is active under most environmental and developmental conditions. An "inducible" promoter is a promoter that is active under environmental or developmental regulation. The term "operably linked" refers to a functional linkage between a nucleic acid expression control sequence (such as a promoter, or array of transcription factor binding sites) and a second nucleic acid sequence, wherein the expression control sequence directs transcription of the nucleic acid corresponding to the second sequence.

An "expression vector" is a nucleic acid construct, generated recombinantly or synthetically, with a series of specified nucleic acid elements that permit transcription of a particular nucleic acid in a host cell. The expression vector can be part of a plasmid, virus, or nucleic acid fragment. Typically, the expression vector includes a nucleic acid to be transcribed operably linked to a promoter.

The phrase "selectively (or specifically) hybridizes to" refers to the binding, duplexing, or hybridizing of a molecule only to a particular nucleotide sequence under stringent hybridization conditions when that sequence is present in a complex mixture (e.g., total cellular or library DNA or RNA).

The phrase "stringent hybridization conditions" refers to conditions under which a probe will hybridize to its target subsequence, typically in a complex mixture of nucleic acids, but to no other sequences. Stringent conditions are sequence-dependent and will be different in different circumstances. Longer sequences hybridize specifically at higher temperatures. An extensive guide to the hybridization of nucleic acids is found in Tijssen, *Techniques in Biochemistry and Molecular Biology--Hybridization with Nucleic Probes*, "Overview of principles of hybridization and the strategy of nucleic acid assays" (1993). Generally, stringent conditions are selected to be about 5-10°C lower than the thermal melting point (T_m) for the specific sequence at a defined ionic strength pH. The T_m is the temperature (under defined ionic strength, pH, and nucleic concentration) at which 50%

of the probes complementary to the target hybridize to the target sequence at equilibrium (as the target sequences are present in excess, at T_m, 50% of the probes are occupied at equilibrium). Stringent conditions will be those in which the salt concentration is less than about 1.0 M sodium ion, typically about 0.01 to 1.0 M sodium ion concentration (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30°C for short probes (e.g., 10 to 50 nucleotides) and at least about 60°C for long probes (e.g., greater than 50 nucleotides). Stringent conditions may also be achieved with the addition of destabilizing agents such as formamide. For selective or specific hybridization, a positive signal is at least two times background, preferably 10 times background hybridization. Exemplary stringent hybridization conditions can be as following: 50% formamide, 5x SSC, and 1% SDS, incubating at 42°C, or, 5x SSC, 1% SDS, incubating at 65°C, with wash in 0.2x SSC, and 0.1% SDS at 65°C. For PCR, a temperature of about 36°C is typical for low stringency amplification, although annealing temperatures may vary between about 32°C and 48°C depending on primer length. For high stringency PCR amplification, a temperature of about 62°C is typical, although high stringency annealing temperatures can range from about 50°C to about 65°C, depending on the primer length and specificity. Typical cycle conditions for both high and low stringency amplifications include a denaturation phase of 90°C - 95°C for 30 sec - 2 min., an annealing phase lasting 30 sec. - 2 min., and an extension phase of about 72°C for 1 - 2 min. Protocols and guidelines for low and high stringency amplification reactions are provided, *e.g.*, in Innis *et al.* (1990) *PCR Protocols, A Guide to Methods and Applications*, Academic Press, Inc. N.Y.).

Nucleic acids that do not hybridize to each other under stringent conditions are still substantially identical if the polypeptides which they encode are substantially identical. This occurs, for example, when a copy of a nucleic acid is created using the maximum codon degeneracy permitted by the genetic code. In such cases, the nucleic acids typically hybridize under moderately stringent hybridization conditions. Exemplary "moderately stringent hybridization conditions" include a hybridization in a buffer of 40% formamide, 1 M NaCl, 1% SDS at 37°C, and a wash in 1X SSC at 45°C. A positive hybridization is at least twice background. Those of ordinary skill will readily recognize that alternative hybridization and wash conditions can be utilized to provide conditions of similar stringency. Additional guidelines for determining hybridization parameters are provided in numerous reference, *e.g.*, and Current Protocols in Molecular Biology, ed. Ausubel, *et al*

The phrase "functional effects" in the context of assays for testing compounds that modulate activity of an angiogenesis protein includes the determination of a parameter that is indirectly or directly under the influence of the angiogenesis protein, *e.g.*, a functional, physical, or chemical effect, such as the ability to increase or decrease angiogenesis. It includes binding activity, the ability of cells to proliferate, expression in cells undergoing angiogenesis, and other characteristics of angiogenic cells. "Functional effects" include *in vitro*, *in vivo*, and *ex vivo* activities.

By "determining the functional effect" is meant assaying for a compound that increases or decreases a parameter that is indirectly or directly under the influence of an angiogenesis protein sequence, *e.g.*, functional, physical and chemical effects. Such functional effects can be measured by any means known to those skilled in the art, *e.g.*, changes in spectroscopic characteristics (*e.g.*, fluorescence, absorbance, refractive index), hydrodynamic (*e.g.*, shape), chromatographic, or solubility properties for the protein, measuring inducible markers or transcriptional activation of the angiogenesis protein; measuring binding activity or binding assays, *e.g.* binding to antibodies, and measuring cellular proliferation, particularly endothelial cell proliferation. Determination of the functional effect of a compound on angiogenesis can also be performed using angiogenesis assays known to those of skill in the art such as an *in vitro* assays, *e.g.*, *in vitro* endothelial cell tube formation assays, and other assays such as the chick CAM assay, the mouse corneal assay, and assays that assess vascularization of an implanted tumor. The functional effects can be evaluated by many means known to those skilled in the art, *e.g.*, microscopy for quantitative or qualitative measures of alterations in morphological features, *e.g.*, tube or blood vessel formation, measurement of changes in RNA or protein levels for angiogenesis-associated sequences, measurement of RNA stability, identification of downstream or reporter gene expression (CAT, luciferase, β-gal, GFP and the like), *e.g.*, via chemiluminescence, fluorescence, colorimetric reactions, antibody binding, inducible markers, and ligand binding assays.

"Inhibitors", "activators", and "modulators" of angiogenic polynucleotide and polypeptide sequences are used to refer to activating, inhibitory, or modulating molecules identified using *in vitro* and *in vivo* assays of angiogenic polynucleotide and polypeptide sequences. Inhibitors are compounds that, *e.g.*, bind to, partially or totally block activity, decrease, prevent, delay activation, inactivate, desensitize, or down regulate the activity or expression of angiogenesis proteins, *e.g.*, antagonists. "Activators" are compounds that increase, open, activate, facilitate, enhance activation, sensitize, agonize, or up regulate

angiogenesis protein activity. Inhibitors, activators, or modulators also include genetically modified versions of angiogenesis proteins, *e.g.*, versions with altered activity, as well as naturally occurring and synthetic ligands, antagonists, agonists, antibodies, small chemical molecules and the like. Such assays for inhibitors and activators include, *e.g.*, expressing the angiogenic protein *in vitro*, in cells, or cell membranes, applying putative modulator compounds, and then determining the functional effects on activity, as described above. Activators and inhibitors of angiogenesis can also be identified by incubating angiogenic cells with the test compound and determining increases or decreases in the expression of 1 or more angiogenesis proteins, *e.g.*, 1, 2, 3, 4, 5, 10, 15, 20, 25, 30, 40, 50 or more angiogenesis proteins, such as angiogenesis proteins comprising the sequences set out in Table 2.

Samples or assays comprising angiogenesis proteins that are treated with a potential activator, inhibitor, or modulator are compared to control samples without the inhibitor, activator, or modulator to examine the extent of inhibition. Control samples (untreated with inhibitors) are assigned a relative protein activity value of 100%. Inhibition of a polypeptide is achieved when the activity value relative to the control is about 80%, preferably 50%, more preferably 25-0%. Activation of an angiogenesis polypeptide is achieved when the activity value relative to the control (untreated with activators) is 110%, more preferably 150%, more preferably 200-500% (i.e., two to five fold higher relative to the control), more preferably 1000-3000% higher.

"Antibody" refers to a polypeptide comprising a framework region from an immunoglobulin gene or fragments thereof that specifically binds and recognizes an antigen. The recognized immunoglobulin genes include the kappa, lambda, alpha, gamma, delta, epsilon, and mu constant region genes, as well as the myriad immunoglobulin variable region genes. Light chains are classified as either kappa or lambda. Heavy chains are classified as gamma, mu, alpha, delta, or epsilon, which in turn define the immunoglobulin classes, IgG, IgM, IgA, IgD and IgE, respectively. Typically, the antigen-binding region of an antibody will be most critical in specificity and affinity of binding.

An exemplary immunoglobulin (antibody) structural unit comprises a tetramer. Each tetramer is composed of two identical pairs of polypeptide chains, each pair having one "light" (about 25 kD) and one "heavy" chain (about 50-70 kD). The $\mathrm{N}^{\prime}$-terminus of each chain defines a variable region of about 100 to 110 or more amino acids primarily responsible for antigen recognition. The terms variable light chain (V_L) and variable heavy chain (V_H) refer to these light and heavy chains respectively.

Antibodies exist, *e.g.*, as intact immunoglobulins or as a number of well-characterized fragments produced by digestion with various peptidases. Thus, for example, pepsin digests an antibody below the disulfide linkages in the hinge region to produce F(ab)'$_2$, a dimer of Fab which itself is a light chain joined to V_H-C_H1 by a disulfide bond. The F(ab)'$_2$ may be reduced under mild conditions to break the disulfide linkage in the hinge region, thereby converting the F(ab)'$_2$ dimer into an Fab' monomer. The Fab' monomer is essentially Fab with part of the hinge region (*see Fundamental Immunology* (Paul ed., 3d ed. 1993). While various antibody fragments are defined in terms of the digestion of an intact antibody, one of skill will appreciate that such fragments may be synthesized *de novo* either chemically or by using recombinant DNA methodology. Thus, the term antibody, as used herein, also includes antibody fragments either produced by the modification of whole antibodies, or those synthesized *de novo* using recombinant DNA methodologies (*e.g.*, single chain Fv) or those identified using phage display libraries (*see, e.g.*, McCafferty *et al.*, *Nature* 348:552-554 (1990))

For preparation of antibodies, *e.g.*, recombinant, monoclonal, or polyclonal antibodies, many technique known in the art can be used (*see, e.g.*, Kohler & Milstein, *Nature* 256:495-497 (1975); Kozbor *et al.*, *Immunology Today* 4: 72 (1983); Cole *et al.*, pp. 77-96 in *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, Inc. (1985); Coligan, *Current Protocols in Immunology* (1991); Harlow & Lane, *Antibodies, A Laboratory Manual* (1988); and Goding, *Monoclonal Antibodies: Principles and Practice* (2d ed. 1986)). Techniques for the production of single chain antibodies (U.S. Patent 4,946,778) can be adapted to produce antibodies to polypeptides of this invention. Also, transgenic mice, or other organisms such as other mammals, may be used to express humanized antibodies. Alternatively, phage display technology can be used to identify antibodies and heteromeric Fab fragments that specifically bind to selected antigens (*see, e.g.*, McCafferty *et al.*, *Nature* 348:552-554 (1990); Marks *et al.*, *Biotechnology* 10:779-783 (1992)).

A "chimeric antibody" is an antibody molecule in which (a) the constant region, or a portion thereof, is altered, replaced or exchanged so that the antigen binding site (variable region) is linked to a constant region of a different or altered class, effector function and/or species or an entirely different molecule which confers new properties to the chimeric antibody, *e.g.*, an enzyme, toxin, hormone, growth factor, drug, etc.; or (b) the variable region, or a portion thereof, is altered, replaced or exchanged with a variable region having a different or altered antigen specificity.

The present application may be related to USSN 09/437,702, filed Nov. 10, 1999; USSN 09/437,528, filed Nov. 10, 1999; USSN 09/434,197, filed Nov. 4, 1999; USSN 60/183,926, filed Feb. 22, 2000; USSN 09/440,493, filed Nov. 15, 1999; USSN 09/520,478, filed Mar. 8, 2000; USSN 09/440,369, filed Nov. 12, 1999; Attorney Docket number A68928, filed Dec. 15, 2000; Attorney Docket number A69789, filed Jan. 22, 2001; and Attorney Docket number A69806, filed Dec. 15, 2000.

The detailed description of the invention includes discussion of the following aspects of the invention:

- Expression of angiogenesis-associated sequences
- Informatics
- Angiogenesis-associated sequences
- Detection of angiogenesis sequence for diagnostic and therapeutic applications
- Modulators of angiogenesis
- Methods of identifying variant angiogenesis-associated sequences
- Administration of pharmaceutical and vaccinecompositions
- Kits for use in diagnostic and/or prognostic applications.

Expression of angiogenesis-associated sequences

In one aspect, the expression levels of genes are determined in different patient samples for which diagnosis information is desired, to provide expression profiles. An expression profile of a particular sample is essentially a "fingerprint" of the state of the sample; while two states may have any particular gene similarly expressed, the evaluation of a number of genes simultaneously allows the generation of a gene expression profile that is unique to the state of the cell. That is, normal tissue may be distinguished from AD tissue. By comparing expression profiles of tissue in known different angiogenesis states, information regarding which genes are important (including both up- and down-regulation of genes) in each of these states is obtained. The identification of sequences that are differentially expressed in angiogenic versus non-angiogenic tissue allows the use of this information in a number of ways. For example, a particular treatment regime may be evaluated: does a chemotherapeutic drug act to down-regulate angiogenesis, and thus tumor growth or recurrence, in a particular patient. Similarly, diagnosis and treatment outcomes may be done or confirmed by comparing patient samples with the known expression profiles. Angiogenic tissue can also be analyzed to determine the stage of angiogenesis in the tissue. Furthermore, these gene expression profiles (or individual genes) allow screening of drug

candidates with an eye to mimicking or altering a particular expression profile; for example, screening can be done for drugs that suppress the angiogenic expression profile. This may be done by making biochips comprising sets of the important angiogenesis genes, which can then be used in these screens. These methods can also be done on the protein basis; that is, protein expression levels of the angiogenic proteins can be evaluated for diagnostic purposes or to screen candidate agents. In addition, the angiogenic nucleic acid sequences can be administered for gene therapy purposes, including the administration of antisense nucleic acids, or the angiogenic proteins (including antibodies and other modulators thereof) administered as therapeutic drugs.

Thus the present invention provides nucleic acid and protein sequences that are differentially expressed in angiogenesis, herein termed "angiogenesis sequences". As outlined below, angiogenesis sequences include those that are up-regulated (i.e. expressed at a higher level) in disorders associated with angiogenesis, as well as those that are down-regulated (i.e. expressed at a lower level). In a preferred embodiment, the angiogenesis sequences are from humans; however, as will be appreciated by those in the art, angiogenesis sequences from other organisms may be useful in animal models of disease and drug evaluation; thus, other angiogenesis sequences are provided, from vertebrates, including mammals, including rodents (rats, mice, hamsters, guinea pigs, etc.), primates, farm animals (including sheep, goats, pigs, cows, horses, etc). Angiogenesis sequences from other organisms may be obtained using the techniques outlined below.

Angiogenesis sequences can include both nucleic acid and amino acid sequences. In a preferred embodiment, the angiogenesis sequences are recombinant nucleic acids. By the term "recombinant nucleic acid" herein is meant nucleic acid, originally formed *in vitro*, in general, by the manipulation of nucleic acid *e.g.*, using polymerases and endonucleases, in a form not normally found in nature. Thus an isolated nucleic acid, in a linear form, or an expression vector formed *in vitro* by ligating DNA molecules that are not normally joined, are both considered recombinant for the purposes of this invention. It is understood that once a recombinant nucleic acid is made and reintroduced into a host cell or organism, it will replicate non-recombinantly, *i.e.* using the *in vivo* cellular machinery of the host cell rather than *in vitro* manipulations; however, such nucleic acids, once produced recombinantly, although subsequently replicated non-recombinantly, are still considered recombinant for the purposes of the invention.

Similarly, a "recombinant protein" is a protein made using recombinant techniques, *i.e.* through the expression of a recombinant nucleic acid as depicted above. A

recombinant protein is distinguished from naturally occurring protein by at least one or more characteristics. For example, the protein may be isolated or purified away from some or all of the proteins and compounds with which it is normally associated in its wild type host, and thus may be substantially pure. For example, an isolated protein is unaccompanied by at least some of the material with which it is normally associated in its natural state, preferably constituting at least about 0.5%, more preferably at least about 5% by weight of the total protein in a given sample. A substantially pure protein comprises at least about 75% by weight of the total protein, with at least about 80% being preferred, and at least about 90% being particularly preferred. The definition includes the production of an angiogenesis protein from one organism in a different organism or host cell. Alternatively, the protein may be made at a significantly higher concentration than is normally seen, through the use of an inducible promoter or high expression promoter, such that the protein is made at increased concentration levels. Alternatively, the protein may be in a form not normally found in nature, as in the addition of an epitope tag or amino acid substitutions, insertions and deletions, as discussed below.

In a preferred embodiment, the angiogenesis sequences are nucleic acids. As will be appreciated by those in the art and is more fully outlined below, angiogenesis sequences are useful in a variety of applications, including diagnostic applications, which will detect naturally occurring nucleic acids, as well as screening applications; for example, biochips comprising nucleic acid probes to the angiogenesis sequences can be generated. In the broadest sense, then, by "nucleic acid" or "oligonucleotide" or grammatical equivalents herein means at least two nucleotides covalently linked together. A nucleic acid of the present invention will generally contain phosphodiester bonds, although in some cases, nucleic acid analogs are included that may have alternate backbones, comprising, for example, phosphoramidate, phosphorothioate, phosphorodithioate, or O-methylphophoroamidite linkages (see Eckstein, Oligonucleotides and Analogues: A Practical Approach, Oxford University Press); and peptide nucleic acid backbones and linkages. Other analog nucleic acids include those with positive backbones; non-ionic backbones, and non-ribose backbones, including those described in U.S. Patent Nos. 5,235,033 and 5,034,506, and Chapters 6 and 7, ASC Symposium Series 580, "Carbohydrate Modifications in Antisense Research", Ed. Y.S. Sanghui and P. Dan Cook. Nucleic acids containing one or more carbocyclic sugars are also included within one definition of nucleic acids. Modifications of the ribose-phosphate backbone may be done for a variety of reasons, for

example to increase the stability and half-life of such molecules in physiological environments or as probes on a biochip.

As will be appreciated by those in the art, nucleic acid analogs may find use in the present invention. In addition, mixtures of naturally occurring nucleic acids and analogs can be made; alternatively, mixtures of different nucleic acid analogs, and mixtures of naturally occurring nucleic acids and analogs may be made.

Particularly preferred are peptide nucleic acids (PNA) which includes peptide nucleic acid analogs. These backbones are substantially non-ionic under neutral conditions, in contrast to the highly charged phosphodiester backbone of naturally occurring nucleic acids. This results in two advantages. First, the PNA backbone exhibits improved hybridization kinetics. PNAs have larger changes in the melting temperature (Tm) for mismatched versus perfectly matched basepairs. DNA and RNA typically exhibit a 2-4°C drop in T_m for an internal mismatch. With the non-ionic PNA backbone, the drop is closer to 7-9°C. Similarly, due to their non-ionic nature, hybridization of the bases attached to these backbones is relatively insensitive to salt concentration. In addition, PNAs are not degraded by cellular enzymes, and thus can be more stable.

The nucleic acids may be single stranded or double stranded, as specified, or contain portions of both double stranded or single stranded sequence. As will be appreciated by those in the art, the depiction of a single strand also defines the sequence of the complementary strand; thus the sequences described herein also provide the complement of the sequence. The nucleic acid may be DNA, both genomic and cDNA, RNA or a hybrid, where the nucleic acid may contain combinations of deoxyribo- and ribo-nucleotides, and combinations of bases, including uracil, adenine, thymine, cytosine, guanine, inosine, xanthine hypoxanthine, isocytosine, isoguanine, etc. As used herein, the term "nucleoside" includes nucleotides and nucleoside and nucleotide analogs, and modified nucleosides such as amino modified nucleosides. In addition, "nucleoside" includes non-naturally occurring analog structures. Thus for example the individual units of a peptide nucleic acid, each containing a base, are referred to herein as a nucleoside.

An angiogenesis sequence can be initially identified by substantial nucleic acid and/or amino acid sequence homology to the angiogenesis sequences outlined herein. Such homology can be based upon the overall nucleic acid or amino acid sequence, and is generally determined as outlined below, using either homology programs or hybridization conditions.

For identifying angiogenesis-associated sequences, the angiogenesis screen typically includes comparing genes identified in a modification of an *in vitro* model of angiogenesis as described in Hiraoka, Cell 95:365 (1998) with genes identified in controls. Samples of normal tissue and tissue undergoing angiogenesis are applied to biochips comprising nucleic acid probes. The samples are first microdissected, if applicable, and treated as is known in the art for the preparation of mRNA. Suitable biochips are commercially available, for example from Affymetrix. Gene expression profiles as described herein are generated and the data analyzed.

In a preferred embodiment, the genes showing changes in expression as between normal and disease states are compared to genes expressed in other normal tissues, including, but not limited to lung, heart, brain, liver, breast, kidney, muscle, prostate, small intestine, large intestine, spleen, bone and placenta. In a preferred embodiment, those genes identified during the angiogenesis screen that are expressed in any significant amount in other tissues are removed from the profile, although in some embodiments, this is not necessary. That is, when screening for drugs, it is usually preferable that the target be disease specific, to minimize possible side effects.

In a preferred embodiment, angiogenesis sequences are those that are up-regulated in angiogenesis disorders; that is, the expression of these genes is higher in the disease tissue as compared to normal tissue. "Up-regulation" as used herein means at least about a two-fold change, preferably at least about a three fold change, with at least about five-fold or higher being preferred. All accession numbers herein are for the GenBank sequence database and the sequences of the accession numbers are hereby expressly incorporated by reference. GenBank is known in the art, see, *e.g.*, Benson, DA, et al., Nucleic Acids Research 26:1-7 (1998) and http://www.ncbi.nlm.nih.gov/. Sequences are also avialable in other databases, *e.g.*, European Molecular Biology Laboratory (EMBL) and DNA Database of Japan (DDBJ). In addition, most preferred genes were found to be expressed in a limited amount or not at all in heart, brain, lung, liver, breast, kidney, prostate, small intestine and spleen.

In another preferred embodiment, angiogenesis sequences are those that are down-regulated in the angiogenesis disorder; that is, the expression of these genes is lower in angiogenic tissue as compared to normal tissue. "Down-regulation" as used herein means at least about a two-fold change, preferably at least about a three fold change, with at least about five-fold or higher being preferred.

Angiogenesis sequences according to the invention may be classified into discrete clusters of sequences based on common expression profiles of the sequences. Expression levels of angiogenesis sequences may increase or decrease as a function of time in a manner that correlates with the induction of angiogenesis. Alternatively, expression levels of angiogenesis sequences may both increase and decrease as a function of time. For example, expression levels of some angiogenesis sequences are temporarily induced or diminished during the switch to the angiogenesis phenotype, followed by a return to baseline expression levels. Table 1 provides genes, the mRNA expression of which varies as a function of time in angiogenesis tissue when compared to normal tissue.

Table 2 provides protein sequences corresponding to the coding regions of the sequences that undergo changes in expression as a function of time in tissue undergoing angiogenesis.

In a particularly preferred embodiment, angiogenesis sequences are those that are induced for a period of time, typically by positive angiogenic factors, followed by a return to the baseline levels. Sequences that are temporarily induced provide a means to target angiogenesis tissue, for example neovascularized tumors, at a particular stage of angiogenesis, while avoiding rapidly growing tissue that require perpetual vascularization. Such positive angiogenic factors include αFGF, βFGF, VEGF, angiogenin and the like.

Induced angiogenesis sequences also are further categorized with respect to the timing of induction. For example, some angiogenesis genes may be induced at an early time period, such as within10 minutes of the induction of angiogenesis. Others may be induced later, such as between 5 and 60 minutes, while yet others may be induced for a time period of about two hours or more followed by a return to baseline expression levels.

In another preferred embodiment are angiogenesis sequences that are inhibited or reduced as a function of time followed by a return to "normal" expression levels. Inhibitors of angiogenesis are examples of molecules that have this expression profile. These sequences also can be further divided into groups depending on the timing of diminished expression. For example, some molecules may display reduced expression within 10 minutes of the induction of angiogenesis. Others may be diminished later, such as between 5 and 60 minutes, while others may be diminished for a time period of about two hours or more followed by a return to baseline. Examples of such negative angiogenic factors include thrombospondin and endostatin to name a few.

In yet another preferred embodiment are angiogenesis sequences that are induced for prolonged periods. These sequences are typically associated with induction of angiogenesis and may participate in induction and/or maintenance of the angiogenesis phenotype.

In another preferred embodiment are angiogenesis sequences, the expression of which is reduced or diminished for prolonged periods in angiogenic tissue. These sequences are typically angiogenesis inhibitors and their diminution is correlated with an increase in angiogenesis.

Informatics

The ability to identify genes that undergo changes in expression with time during angiogenesis can additionally provide high-resolution, high-sensitivity datasets which can be used in the areas of diagnostics, therapeutics, drug development, biosensor development, and other related areas. For example, the expression profiles can be used in diagnostic or prognostic evaluation of patients with angiogenesis-associated disease. Or as another example, subcellular toxicological information can be generated to better direct drug structure and activity correlation (*see*, Anderson, L., "Pharmaceutical Proteomics: Targets, Mechanism, and Function," paper presented at the IBC Proteomics conference, Coronado, CA (June 11-12, 1998)). Subcellular toxicological information can also be utilized in a biological sensor device to predict the likely toxicological effect of chemical exposures and likely tolerable exposure thresholds (*see*, U.S. Patent No. 5,811,231). Similar advantages accrue from datasets relevant to other biomolecules and bioactive agents (*e.g.*, nucleic acids, saccharides, lipids, drugs, and the like).

Thus, in another embodiment, the present invention provides a database that includes at least one set of data assay data. The data contained in the database is acquired , *e.g.*, using array analysis either singly or in a library format. The database can be in substantially any form in which data can be maintained and transmitted, but is preferably an electronic database. The electronic database of the invention can be maintained on any electronic device allowing for the storage of and access to the database, such as a personal computer, but is preferably distributed on a wide area network, such as the World Wide Web.

The focus of the present section on databases that include peptide sequence data is for clarity of illustration only. It will be apparent to those of skill in the art that similar databases can be assembled for any assay data acquired using an assay of the invention.

The compositions and methods for identifying and/or quantitating the relative and/or absolute abundance of a variety of molecular and macromolecular species from a biological sample undergoing angiogenesis, *i.e.*, the identification of angiogenesis-associated sequences described herein, provide an abundance of information, which can be correlated with pathological conditions, predisposition to disease, drug testing, therapeutic monitoring, gene-disease causal linkages, identification of correlates of immunity and physiological status, among others. Although the data generated from the assays of the invention is suited for manual review and analysis, in a preferred embodiment, prior data processing using high-speed computers is utilized.

An array of methods for indexing and retrieving biomolecular information is known in the art. For example, U.S. Patents 6,023,659 and 5,966,712 disclose a relational database system for storing biomolecular sequence information in a manner that allows sequences to be catalogued and searched according to one or more protein function hierarchies. U.S. Patent 5,953,727 discloses a relational database having sequence records containing information in a format that allows a collection of partial-length DNA sequences to be catalogued and searched according to association with one or more sequencing projects for obtaining full-length sequences from the collection of partial length sequences. U.S. Patent 5,706,498 discloses a gene database retrieval system for making a retrieval of a gene sequence similar to a sequence data item in a gene database based on the degree of similarity between a key sequence and a target sequence. U.S. Patent 5,538,897 discloses a method using mass spectroscopy fragmentation patterns of peptides to identify amino acid sequences in computer databases by comparison of predicted mass spectra with experimentally-derived mass spectra using a closeness-of-fit measure. U.S. Patent 5,926,818 discloses a multi-dimensional database comprising a functionality for multi-dimensional data analysis described as on-line analytical processing (OLAP), which entails the consolidation of projected and actual data according to more than one consolidation path or dimension. U.S. Patent 5,295,261 reports a hybrid database structure in which the fields of each database record are divided into two classes, navigational and informational data, with navigational fields stored in a hierarchical topological map which can be viewed as a tree structure or as the merger of two or more such tree structures.

The present invention provides a computer database comprising a computer and software for storing in computer-retrievable form assay data records cross-tabulated, *e.g.*, with data specifying the source of the target-containing sample from which each sequence specificity record was obtained.

In an exemplary embodiment, at least one of the sources of target-containing sample is from a control tissue sample known to be free of pathological disorders. In a variation, at least one of the sources is a known pathological tissue specimen, *e.g.*, a neoplastic lesion or another tissue specimen to be analyzed for angiogenesis. In another variation, the assay records cross-tabulate one or more of the following parameters for each target species in a sample: (1) a unique identification code, which can include, *e.g.*, a target molecular structure and/or characteristic separation coordinate (*e.g.*, electrophoretic coordinates); (2) sample source; and (3) absolute and/or relative quantity of the target species present in the sample.

The invention also provides for the storage and retrieval of a collection of target data in a computer data storage apparatus, which can include magnetic disks, optical disks, magneto-optical disks, DRAM, SRAM, SGRAM, SDRAM, RDRAM, DDR RAM, magnetic bubble memory devices, and other data storage devices, including CPU registers and on-CPU data storage arrays. Typically, the target data records are stored as a bit pattern in an array of magnetic domains on a magnetizable medium or as an array of charge states or transistor gate states, such as an array of cells in a DRAM device (*e.g.*, each cell comprised of a transistor and a charge storage area, which may be on the transistor). In one embodiment, the invention provides such storage devices, and computer systems built therewith, comprising a bit pattern encoding a protein expression fingerprint record comprising unique identifiers for at least 10 target data records cross-tabulated with target source.

When the target is a peptide or nucleic acid, the invention preferably provides a method for identifying related peptide or nucleic acid sequences, comprising performing a computerized comparison between a peptide or nucleic acid sequence assay record stored in or retrieved from a computer storage device or database and at least one other sequence. The comparison can include a sequence analysis or comparison algorithm or computer program embodiment thereof (*e.g.*, FASTA, TFASTA, GAP, BESTFIT) and/or the comparison may be of the relative amount of a peptide or nucleic acid sequence in a pool of sequences determined from a polypeptide or nucleic acid sample of a specimen.

The invention also preferably provides a magnetic disk, such as an IBM-compatible (DOS, Windows, Windows95/98/2000, Windows NT, OS/2) or other format (*e.g.*, Linux, SunOS, Solaris, AIX, SCO Unix, VMS, MV, Macintosh, *etc.*) floppy diskette or hard (fixed, Winchester) disk drive, comprising a bit pattern encoding data from an assay of the invention in a file format suitable for retrieval and processing in a computerized sequence analysis, comparison, or relative quantitation method.

The invention also provides a network, comprising a plurality of computing devices linked via a data link, such as an Ethernet cable (coax or 10BaseT), telephone line, ISDN line, wireless network, optical fiber, or other suitable signal tranmission medium, whereby at least one network device (*e.g.*, computer, disk array, *etc.*) comprises a pattern of magnetic domains (*e.g.*, magnetic disk) and/or charge domains (*e.g.*, an array of DRAM cells) composing a bit pattern encoding data acquired from an assay of the invention.

The invention also provides a method for transmitting assay data that includes generating an electronic signal on an electronic communications device, such as a modem, ISDN terminal adapter, DSL, cable modem, ATM switch, or the like, wherein the signal includes (in native or encrypted format) a bit pattern encoding data from an assay or a database comprising a plurality of assay results obtained by the method of the invention.

In a preferred embodiment, the invention provides a computer system for comparing a query target to a database containing an array of data structures, such as an assay result obtained by the method of the invention, and ranking database targets based on the degree of identity and gap weight to the target data. A central processor is preferably initialized to load and execute the computer program for alignment and/or comparison of the assay results. Data for a query target is entered into the central processor via an I/O device. Execution of the computer program results in the central processor retrieving the assay data from the data file, which comprises a binary description of an assay result.

The target data or record and the computer program can be transferred to secondary memory, which is typically random access memory (*e.g.*, DRAM, SRAM, SGRAM, or SDRAM). Targets are ranked according to the degree of correspondence between a selected assay characteristic (*e.g.*, binding to a selected affinity moiety) and the same characteristic of the query target and results are output via an I/O device. For example, a central processor can be a conventional computer (*e.g.*, Intel Pentium, PowerPC, Alpha, PA-8000, SPARC, MIPS 4400, MIPS 10000, VAX, *etc.*); a program can be a commercial or public domain molecular biology software package (*e.g.*, UWGCG Sequence Analysis Software, Darwin); a data file can be an optical or magnetic disk, a data server, a memory device (*e.g.*, DRAM, SRAM, SGRAM, SDRAM, EPROM, bubble memory, flash memory, *etc.*); an I/O device can be a terminal comprising a video display and a keyboard, a modem, an ISDN terminal adapter, an Ethernet port, a punched card reader, a magnetic strip reader, or other suitable I/O device.

The invention also preferably provides the use of a computer system, such as that described above, which comprises: (1) a computer; (2) a stored bit pattern encoding a

collection of peptide sequence specificity records obtained by the methods of the invention, which may be stored in the computer; (3) a comparison target, such as a query target; and (4) a program for alignment and comparison, typically with rank-ordering of comparison results on the basis of computed similarity values.

Angiogenesis-associated sequences

Angiogenesis proteins of the present invention may be classified as secreted proteins, transmembrane proteins or intracellular proteins. In one embodiment,the angiogenesis protein is an intracellular protein. Intracellular proteins may be found in the cytoplasm and/or in the nucleus. Intracellular proteins are involved in all aspects of cellular function and replication (including, *e.g.*, signaling pathways); aberrant expression of such proteins often results in unregulated or disregulated cellular processes (see, *e.g.*, Molecular Biology of the Cell, 3rd Edition, Alberts, Ed., Garland Pub., 1994). For example, many intracellular proteins have enzymatic activity such as protein kinase activity, protein phosphatase activity, protease activity, nucleotide cyclase activity, polymerase activity and the like. Intracellular proteins also serve as docking proteins that are involved in organizing complexes of proteins, or targeting proteins to various subcellular localizations, and are involved in maintaining the structural integrity of organelles.

An increasingly appreciated concept in characterizing proteins is the presence in the proteins of one or more motifs for which defined functions have been attributed. In addition to the highly conserved sequences found in the enzymatic domain of proteins, highly conserved sequences have been identified in proteins that are involved in protein-protein interaction. For example, Src-homology-2 (SH2) domains bind tyrosine-phosphorylated targets in a sequence dependent manner. PTB domains, which are distinct from SH2 domains, also bind tyrosine phosphorylated targets. SH3 domains bind to proline-rich targets. In addition, PH domains, tetratricopeptide repeats and WD domains to name only a few, have been shown to mediate protein-protein interactions. Some of these may also be involved in binding to phospholipids or other second messengers. As will be appreciated by one of ordinary skill in the art, these motifs can be identified on the basis of primary sequence; thus, an analysis of the sequence of proteins may provide insight into both the enzymatic potential of the molecule and/or molecules with which the protein may associate.

In another embodiment, the angiogenesis sequences are transmembrane proteins. Transmembrane proteins are molecules that span a phospholipid bilayer of a cell. They may have an intracellular domain, an extracellular domain, or both. The intracellular

domains of such proteins may have a number of functions including those already described for intracellular proteins. For example, the intracellular domain may have enzymatic activity and/or may serve as a binding site for additional proteins. Frequently the intracellular domain of transmembrane proteins serves both roles. For example certain receptor tyrosine kinases have both protein kinase activity and SH2 domains. In addition, autophosphorylation of tyrosines on the receptor molecule itself, creates binding sites for additional SH2 domain containing proteins.

Transmembrane proteins may contain from one to many transmembrane domains. For example, receptor tyrosine kinases, certain cytokine receptors, receptor guanylyl cyclases and receptor serine/threonine protein kinases contain a single transmembrane domain. However, various other proteins including channels and adenylyl cyclases contain numerous transmembrane domains. Many important cell surface receptors such as G protein coupled receptors (GPCRs) are classified as "seven transmembrane domain" proteins, as they contain 7 membrane spanning regions. Characteristics of transmembrane domains include approximately 20 consecutive hydrophobic amino acids that may be followed by charged amino acids. Therefore, upon analysis of the amino acid sequence of a particular protein, the localization and number of transmembrane domains within the protein may be predicted (see, *e.g.* PSORT web site http://psort.nibb.ac.jp/).

The extracellular domains of transmembrane proteins are diverse; however, conserved motifs are found repeatedly among various extracellular domains. Conserved structure and/or functions have been ascribed to different extracellular motifs. Many extracellular domains are involved in binding to other molecules. In one aspect, extracellular domains are found on receptors. Factors that bind the receptor domain include circulating ligands, which may be peptides, proteins, or small molecules such as adenosine and the like. For example, growth factors such as EGF, FGF and PDGF are circulating growth factors that bind to their cognate receptors to initiate a variety of cellular responses. Other factors include cytokines, mitogenic factors, neurotrophic factors and the like. Extracellular domains also bind to cell-associated molecules. In this respect, they mediate cell-cell interactions. Cell-associated ligands can be tethered to the cell for example via a glycosylphosphatidylinositol (GPI) anchor, or may themselves be transmembrane proteins. Extracellular domains also associate with the extracellular matrix and contribute to the maintenance of the cell structure.

Angiogenesis proteins that are transmembrane are particularly preferred in the present invention as they are readily accessible targets for immunotherapeutics, as are described herein. In addition, as outlined below, transmembrane proteins can be also useful

in imaging modalities. Antibodies may be used to label such readily accessible proteins *in situ*. Alternatively, antibodies can also label intracellular proteins, in which case samples are typically permeablized to provide acess to intracellular proteins.

It will also be appreciated by those in the art that a transmembrane protein can be made soluble by removing transmembrane sequences, for example through recombinant methods. Furthermore, transmembrane proteins that have been made soluble can be made to be secreted through recombinant means by adding an appropriate signal sequence.

In another embodiment, the angiogenesis proteins are secreted proteins; the secretion of which can be either constitutive or regulated. These proteins have a signal peptide or signal sequence that targets the molecule to the secretory pathway. Secreted proteins are involved in numerous physiological events; by virtue of their circulating nature, they serve to transmit signals to various other cell types. The secreted protein may function in an autocrine manner (acting on the cell that secreted the factor), a paracrine manner (acting on cells in close proximity to the cell that secreted the factor) or an endocrine manner (acting on cells at a distance). Thus secreted molecules find use in modulating or altering numerous aspects of physiology. Angiogenesis proteins that are secreted proteins are particularly preferred in the present invention as they serve as good targets for diagnostic markers, *e.g.*, for blood or serum tests.

An angiogenesis sequence is initially identified by substantial nucleic acid and/or amino acid sequence homology or linkage to the angiogenesis sequences outlined herein. Such homology can be based upon the overall nucleic acid or amino acid sequence, and is generally determined as outlined below, using either homology programs or hybridization conditions. Typically, linked sequences on a mRNA are found on the same molecule.

As detailed in the definitions, percent identity can be determined using an algorithm such as BLAST. A preferred method utilizes the BLASTN module of WU-BLAST-2 set to the default parameters, with overlap span and overlap fraction set to 1 and 0.125, respectively. The alignment may include the introduction of gaps in the sequences to be aligned. In addition, for sequences which contain either more or fewer nucleotides than those of the nucleic acids of the figures, it is understood that the percentage of homology will be determined based on the number of homologous nucleosides in relation to the total number of nucleosides. Thus, for example, homology of sequences shorter than those of the sequences identified herein and as discussed below, will be determined using the number of nucleosides in the shorter sequence.

In one embodiment, the nucleic acid homology is determined through hybridization studies. Thus, *e.g.*, nucleic acids which hybridize under high stringency to a nucleic acidof Table 1, or its complement, or is also found on naturally occurring mRNAs is considered an angiogenesis sequence. In another embodiment, less stringent hybridization conditions are used; for example, moderate or low stringency conditions may be used, as are known in the art; see Ausubel, *supra*, and Tijssen, *supra*.

In addition, the angiogenesis nucleic acid sequences of the invention, e.g, the sequence in Table 1, are fragments of larger genes, *i.e.* they are nucleic acid segments. "Genes" in this context includes coding regions, non-coding regions, and mixtures of coding and non-coding regions. Accordingly, as will be appreciated by those in the art, using the sequences provided herein, extended sequences, in either direction, of the angiogenesis genes can be obtained, using techniques well known in the art for cloning either longer sequences or the full length sequences; see Ausubel, *et al.*, *supra*. Much can be done by informatics and many sequences can be clustered to include multiple sequences, *e.g.*, systems such as UniGene (see, http://www.ncbi.nlm.nih.gov/UniGene/).

Once the angiogenesis nucleic acid is identified, it can be cloned and, if necessary, its constituent parts recombined to form the entire angiogenesis nucleic acid coding regions or the entire mRNA sequence. Once isolated from its natural source, *e.g.*, contained within a plasmid or other vector or excised therefrom as a linear nucleic acid segment, the recombinant angiogenesis nucleic acid can be further-used as a probe to identify and isolate other angiogenesis nucleic acids, for example extended coding regions. It can also be used as a "precursor" nucleic acid to make modified or variant angiogenesis nucleic acids and proteins.

The angiogenesis nucleic acids of the present invention are used in several ways. In a first embodiment, nucleic acid probes to the angiogenesis nucleic acids are made and attached to biochips to be used in screening and diagnostic methods, as outlined below, or for administration, for example for gene therapy, vaccine, and/or antisense applications. Alternatively, the angiogenesis nucleic acids that include coding regions of angiogenesis proteins can be put into expression vectors for the expression of angiogenesis proteins, again for screening purposes or for administration to a patient.

In a preferred embodiment, nucleic acid probes to angiogenesis nucleic acids (both the nucleic acid sequences outlined in the figures and/or the complements thereof) are made. The nucleic acid probes attached to the biochip are designed to be substantially complementary to the angiogenesis nucleic acids, *i.e.* the target sequence (either the target

sequence of the sample or to other probe sequences, for example in sandwich assays), such that hybridization of the target sequence and the probes of the present invention occurs. As outlined below, this complementarity need not be perfect; there may be any number of base pair mismatches which will interfere with hybridization between the target sequence and the single stranded nucleic acids of the present invention. However, if the number of mutations is so great that no hybridization can occur under even the least stringent of hybridization conditions, the sequence is not a complementary target sequence. Thus, by "substantially complementary" herein is meant that the probes are sufficiently complementary to the target sequences to hybridize under normal reaction conditions, particularly high stringency conditions, as outlined herein.

A nucleic acid probe is generally single stranded but can be partially single and partially double stranded. The strandedness of the probe is dictated by the structure, composition, and properties of the target sequence. In general, the nucleic acid probes range from about 8 to about 100 bases long, with from about 10 to about 80 bases being preferred, and from about 30 to about 50 bases being particularly preferred. That is, generally whole genes are not used. In some embodiments, much longer nucleic acids can be used, up to hundreds of bases.

In a preferred embodiment, more than one probe per sequence is used, with either overlapping probes or probes to different sections of the target being used. That is, two, three, four or more probes, with three being preferred, are used to build in a redundancy for a particular target. The probes can be overlapping (*i.e.* have some sequence in common), or separate. In some cases, PCR primers may be used to amplify signal for higher sensitivity.

As will be appreciated by those in the art, nucleic acids can be attached or immobilized to a solid support in a wide variety of ways. By "immobilized" and grammatical equivalents herein is meant the association or binding between the nucleic acid probe and the solid support is sufficient to be stable under the conditions of binding, washing, analysis, and removal as outlined below. The binding can typically be covalent or non-covalent. By "non-covalent binding" and grammatical equivalents herein is meant one or more of electrostatic, hydrophilic, and hydrophobic interactions. Included in non-covalent binding is the covalent attachment of a molecule, such as, streptavidin to the support and the non-covalent binding of the biotinylated probe to the streptavidin. By "covalent binding" and grammatical equivalents herein is meant that the two moieties, the solid support and the probe, are attached by at least one bond, including sigma bonds, pi bonds and coordination bonds. Covalent bonds can be formed directly between the probe and the solid support or can be

formed by a cross linker or by inclusion of a specific reactive group on either the solid support or the probe or both molecules. Immobilization may also involve a combination of covalent and non-covalent interactions.

In general, the probes are attached to the biochip in a wide variety of ways, as will be appreciated by those in the art. As described herein, the nucleic acids can either be synthesized first, with subsequent attachment to the biochip, or can be directly synthesized on the biochip.

The biochip comprises a suitable solid substrate. By "substrate" or "solid support" or other grammatical equivalents herein is meant a material that can be modified to contain discrete individual sites appropriate for the attachment or association of the nucleic acid probes and is amenable to at least one detection method. As will be appreciated by those in the art, the number of possible substrates are very large, and include, but are not limited to, glass and modified or functionalized glass, plastics (including acrylics, polystyrene and copolymers of styrene and other materials, polypropylene, polyethylene, polybutylene, polyurethanes, TeflonJ, etc.), polysaccharides, nylon or nitrocellulose, resins, silica or silica-based materials including silicon and modified silicon, carbon, metals, inorganic glasses, plastics, etc. In general, the substrates allow optical detection and do not appreciably fluorescese. A preferred substrate is described in copending application entitled Reusable Low Fluorescent Plastic Biochip, U.S. Application Serial No. 09/270,214, filed March 15, 1999, herein incorporated by reference in its entirety.

Generally the substrate is planar, although as will be appreciated by those in the art, other configurations of substrates may be used as well. For example, the probes may be placed on the inside surface of a tube, for flow-through sample analysis to minimize sample volume. Similarly, the substrate may be flexible, such as a flexible foam, including closed cell foams made of particular plastics.

In a preferred embodiment, the surface of the biochip and the probe may be derivatized with chemical functional groups for subsequent attachment of the two. Thus, for example, the biochip is derivatized with a chemical functional group including, but not limited to, amino groups, carboxy groups, oxo groups and thiol groups, with amino groups being particularly preferred. Using these functional groups, the probes can be attached using functional groups on the probes. For example, nucleic acids containing amino groups can be attached to surfaces comprising amino groups, for example using linkers as are known in the art; for example, homo-or hetero-bifunctional linkers as are well known (see 1994 Pierce Chemical Company catalog, technical section on cross-linkers, pages 155-200, incorporated

herein by reference). In addition, in some cases, additional linkers, such as alkyl groups (including substituted and heteroalkyl groups) may be used.

In this embodiment, oligonucleotides are synthesized as is known in the art, and then attached to the surface of the solid support. As will be appreciated by those skilled in the art, either the 5' or 3' terminus may be attached to the solid support, or attachment may be via an internal nucleoside.

In another embodiment, the immobilization to the solid support may be very strong, yet non-covalent. For example, biotinylated oligonucleotides can be made, which bind to surfaces covalently coated with streptavidin, resulting in attachment.

Alternatively, the oligonucleotides may be synthesized on the surface, as is known in the art. For example, photoactivation techniques utilizing photopolymerization compounds and techniques are used. In a preferred embodiment, the nucleic acids can be synthesized in situ, using well known photolithographic techniques, such as those described in WO 95/25116; WO 95/35505; U.S. Patent Nos. 5,700,637 and 5,445,934; and references cited within, all of which are expressly incorporated by reference; these methods of attachment form the basis of the Affimetrix GeneChip™ technology.

Often, amplification-based assays are performed to measure the expression level of angiogenesis-associated sequences. These assays are typically performed in conjunction with reverse transcription. In such assays, an angiogenesis-associated nucleic acid sequence acts as a template in an amplification reaction (*e.g.*, Polymerase Chain Reaction, or PCR). In a quantitative amplification, the amount of amplification product will be proportional to the amount of template in the original sample. Comparison to appropriate controls provides a measure of the amount of angiogenesis-associated RNA. Methods of quantitative amplification are well known to those of skill in the art. Detailed protocols for quantitative PCR are provided, *e.g.*, in Innis *et al.* (1990) *PCR Protocols, A Guide to Methods and Applications*, Academic Press, Inc. N.Y.).

In some embodiments, a TaqMan based assay is used to measure expression. TaqMan based assays use a fluorogenic oligonucleotide probe that contains a 5' fluorescent dye and a 3' quenching agent. The probe hybridizes to a PCR product, but cannot itself be extended due to a blocking agent at the 3' end. When the PCR product is amplified in subsequent cycles, the 5' nuclease activity of the polymerase, *e.g.*, AmpliTaq, results in the cleavage of the TaqMan probe. This cleavage separates the 5' fluorescent dye and the 3' quenching agent, thereby resulting in an increase in fluorescence as a function of

amplification (*see*, for example, literature provided by Perkin-Elmer, *e.g.*, www2.perkin-elmer.com).

Other suitable amplification methods include, but are not limited to, ligase chain reaction (LCR) (*see*, Wu and Wallace (1989) *Genomics* 4: 560, Landegren *et al.* (1988) *Science* 241: 1077, and Barringer *et al.* (1990) *Gene* 89: 117), transcription amplification (Kwoh *et al.* (1989) *Proc. Natl. Acad. Sci. USA* 86: 1173), self-sustained sequence replication (Guatelli *et al.* (1990) *Proc. Nat. Acad. Sci. USA* 87: 1874), dot PCR, and linker adapter PCR, *etc.*

In a preferred embodiment, angiogenesis nucleic acids, *e.g.*, encoding angiogenesis proteins are used to make a variety of expression vectors to express angiogenesis proteins which can then be used in screening assays, as described below. Expression vectors and recombinant DNA technology are well known to those of skill in the art (*see*, *e.g.*, Ausubel, *supra*, and Gene Expression Systems, Fernandez & Hoeffler, Eds, Academic Press, 1999) and are used to express proteins. The expression vectors may be either self-replicating extrachromosomal vectors or vectors which integrate into a host genome. Generally, these expression vectors include transcriptional and translational regulatory nucleic acid operably linked to the nucleic acid encoding the angiogenesis protein. The term "control sequences" refers to DNA sequences used for the expression of an operably linked coding sequence in a particular host organism. Control sequences that are suitable for prokaryotes, for example, include a promoter, optionally an operator sequence, and a ribosome binding site. Eukaryotic cells are known to utilize promoters, polyadenylation signals, and enhancers.

Nucleic acid is "operably linked" when it is placed into a functional relationship with another nucleic acid sequence. For example, DNA for a presequence or secretory leader is operably linked to DNA for a polypeptide if it is expressed as a preprotein that participates in the secretion of the polypeptide; a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the sequence; or a ribosome binding site is operably linked to a coding sequence if it is positioned so as to facilitate translation. Generally, "operably linked" means that the DNA sequences being linked are contiguous, and, in the case of a secretory leader, contiguous and in reading phase. However, enhancers do not have to be contiguous. Linking is typically accomplished by ligation at convenient restriction sites. If such sites do not exist, synthetic oligonucleotide adaptors or linkers are used in accordance with conventional practice. Transcriptional and translational regulatory nucleic acid will generally be appropriate to the host cell used to express the angiogenesis

protein; for example, transcriptional and translational regulatory nucleic acid sequences from Bacillus are preferably used to express the angiogenesis protein in Bacillus. Numerous types of appropriate expression vectors, and suitable regulatory sequences are known in the art for a variety of host cells.

In general, transcriptional and translational regulatory sequences may include, but are not limited to, promoter sequences, ribosomal binding sites, transcriptional start and stop sequences, translational start and stop sequences, and enhancer or activator sequences. In a preferred embodiment, the regulatory sequences include a promoter and transcriptional start and stop sequences.

Promoter sequences encode either constitutive or inducible promoters. The promoters may be either naturally occurring promoters or hybrid promoters. Hybrid promoters, which combine elements of more than one promoter, are also known in the art, and are useful in the present invention.

In addition, an expression vector may comprise additional elements. For example, the expression vector may have two replication systems, thus allowing it to be maintained in two organisms, for example in mammalian or insect cells for expression and in a procaryotic host for cloning and amplification. Furthermore, for integrating expression vectors, the expression vector contains at least one sequence homologous to the host cell genome, and preferably two homologous sequences which flank the expression construct. The integrating vector may be directed to a specific locus in the host cell by selecting the appropriate homologous sequence for inclusion in the vector. Constructs for integrating vectors are well known in the art (*e.g.*, Fernandez & Hoeffler, *supra*).

In addition, in a preferred embodiment, the expression vector contains a selectable marker gene to allow the selection of transformed host cells. Selection genes are well known in the art and will vary with the host cell used.

The angiogenesis proteins of the present invention are produced by culturing a host cell transformed with an expression vector containing nucleic acid encoding an angiogenesis protein, under the appropriate conditions to induce or cause expression of the angiogenesis protein. Conditions appropriate for angiogenesis protein expression will vary with the choice of the expression vector and the host cell, and will be easily ascertained by one skilled in the art through routine experimentation or optimization. For example, the use of constitutive promoters in the expression vector will require optimizing the growth and proliferation of the host cell, while the use of an inducible promoter requires the appropriate growth conditions for induction. In addition, in some embodiments, the timing of the harvest

is important. For example, the baculoviral systems used in insect cell expression are lytic viruses, and thus harvest time selection can be crucial for product yield.

Appropriate host cells include yeast, bacteria, archaebacteria, fungi, and insect and animal cells, including mammalian cells. Of particular interest are *Saccharomyces cerevisiae* and other yeasts, *E. coli, Bacillus subtilis*, Sf9 cells, C129 cells, 293 cells, *Neurospora*, BHK, CHO, COS, HeLa cells, HUVEC (human umbilical vein endothelial cells), THP1 cells (a macrophage cell line) and various other human cells and cell lines.

In a preferred embodiment, the angiogenesis proteins are expressed in mammalian cells. Mammalian expression systems are also known in the art, and include retroviral and adenoviral systems. Of particular use as mammalian promoters are the promoters from mammalian viral genes, since the viral genes are often highly expressed and have a broad host range. Examples include the SV40 early promoter, mouse mammary tumor virus LTR promoter, adenovirus major late promoter, herpes simplex virus promoter, and the CMV promoter (see, *e.g.*, Fernandez & Hoeffler, *supra*). Typically, transcription termination and polyadenylation sequences recognized by mammalian cells are regulatory regions located 3' to the translation stop codon and thus, together with the promoter elements, flank the coding sequence. Examples of transcription terminator and polyadenlytion signals include those derived form SV40.

The methods of introducing exogenous nucleic acid into mammalian hosts, as well as other hosts, is well known in the art, and will vary with the host cell used. Techniques include dextran-mediated transfection, calcium phosphate precipitation, polybrene mediated transfection, protoplast fusion, electroporation, viral infection, encapsulation of the polynucleotide(s) in liposomes, and direct microinjection of the DNA into nuclei.

In a preferred embodiment, angiogenesis proteins are expressed in bacterial systems. Bacterial expression systems are well known in the art. Promoters from bacteriophage may also be used and are known in the art. In addition, synthetic promoters and hybrid promoters are also useful; for example, the tac promoter is a hybrid of the trp and lac promoter sequences. Furthermore, a bacterial promoter can include naturally occurring promoters of non-bacterial origin that have the ability to bind bacterial RNA polymerase and initiate transcription. In addition to a functioning promoter sequence, an efficient ribosome binding site is desirable. The expression vector may also include a signal peptide sequence that provides for secretion of the angiogenesis protein in bacteria. The protein is either

secreted into the growth media (gram-positive bacteria) or into the periplasmic space, located between the inner and outer membrane of the cell (gram-negative bacteria). The bacterial expression vector may also include a selectable marker gene to allow for the selection of bacterial strains that have been transformed. Suitable selection genes include genes which render the bacteria resistant to drugs such as ampicillin, chloramphenicol, erythromycin, kanamycin, neomycin and tetracycline. Selectable markers also include biosynthetic genes, such as those in the histidine, tryptophan and leucine biosynthetic pathways. These components are assembled into expression vectors. Expression vectors for bacteria are well known in the art, and include vectors for *Bacillus subtilis, E. coli, Streptococcus cremoris,* and *Streptococcus lividans*, among others (*e.g.*, Fernandez & Hoeffler, *supra*). The bacterial expression vectors are transformed into bacterial host cells using techniques well known in the art, such as calcium chloride treatment, electroporation, and others.

In one embodiment, angiogenesis proteins are produced in insect cells. Expression vectors for the transformation of insect cells, and in particular, baculovirus-based expression vectors, are well known in the art.

In a preferred embodiment, angiogenesis protein is produced in yeast cells. Yeast expression systems are well known in the art, and include expression vectors for *Saccharomyces cerevisiae, Candida albicans* and *C. maltosa, Hansenula polymorpha, Kluyveromyces fragilis* and *K. lactis, Pichia guillerimondii and P. pastoris, Schizosaccharomyces pombe*, and *Yarrowia lipolytica*.

The angiogenesis protein may also be made as a fusion protein, using techniques well known in the art. Thus, for example, for the creation of monoclonal antibodies, if the desired epitope is small, the angiogenesis protein may be fused to a carrier protein to form an immunogen. Alternatively, the angiogenesis protein may be made as a fusion protein to increase expression, or for other reasons. For example, when the angiogenesis protein is an angiogenesis peptide, the nucleic acid encoding the peptide may be linked to other nucleic acid for expression purposes.

In one embodiment, the angiogenesis nucleic acids, proteins and antibodies of the invention are labeled. By "labeled" herein is meant that a compound has at least one element, isotope or chemical compound attached to enable the detection of the compound. In general, labels fall into three classes: a) isotopic labels, which may be radioactive or heavy isotopes; b) immune labels, which may be antibodies or antigens; and c) colored or fluorescent dyes. The labels may be incorporated into the angiogenesis nucleic acids, proteins and antibodies at any position. For example, the label should be capable of

producing, either directly or indirectly, a detectable signal. The detectable moiety may be a radioisotope, such as ^{3}H, ^{14}C, ^{32}P, ^{35}S, or ^{125}I, a fluorescent or chemiluminescent compound, such as fluorescein isothiocyanate, rhodamine, or luciferin, or an enzyme, such as alkaline phosphatase, beta-galactosidase or horseradish peroxidase. Any method known in the art for conjugating the antibody to the label may be employed, including those methods described by Hunter et al., Nature, 144:945 (1962); David et al., Biochemistry, 13:1014 (1974); Pain et al., J. Immunol. Meth., 40:219 (1981); and Nygren, J. Histochem. and Cytochem., 30:407 (1982).

Accordingly, the present invention also provides angiogenesis protein sequences. An angiogenesis protein of the present invention may be identified in several ways. "Protein" in this sense includes proteins, polypeptides, and peptides. As will be appreciated by those in the art, the nucleic acid sequences of the invention can be used to generate protein sequences. There are a variety of ways to do this, including cloning the entire gene and verifying its frame and amino acid sequence, or by comparing it to known sequences to search for homology to provide a frame, assuming the angiogenesis protein has an identifiable motif or homology to some protein in the database being used. Generally, the nucleic acid sequences are input into a program that will search all three frames for homology. This is done in a preferred embodiment using the following NCBI Advanced BLAST parameters. The program is blastx or blastn. The database is nr. The input data is as "Sequence in FASTA format". The organism list is "none". The "expect" is 10; the filter is default. The "descriptions" is 500, the "alignments" is 500, and the "alignment view" is pairwise. The "Query Genetic Codes" is standard (1). The matrix is BLOSUM62; gap existence cost is 11, per residue gap cost is 1; and the lambda ratio is .85 default. This results in the generation of a putative protein sequence.

Also included within one embodiment of angiogenesis proteins are amino acid variants of the naturally occurring sequences, as determined herein. Preferably, the variants are preferably greater than about 75% homologous to the wild-type sequence, more preferably greater than about 80%, even more preferably greater than about 85% and most preferably greater than 90%. In some embodiments the homology will be as high as about 93 to 95 or 98%. As for nucleic acids, homology in this context means sequence similarity or identity, with identity being preferred. This homology will be determined using standard techniques well known in the art as are outlined above for the nucleic acid homologies.

Angiogenesis proteins of the present invention may be shorter or longer than the wild type amino acid sequences. Thus, in a preferred embodiment, included within the

definition of angiogenesis proteins are portions or fragments of the wild type sequences. herein. In addition, as outlined above, the angiogenesis nucleic acids of the invention may be used to obtain additional coding regions, and thus additional protein sequence, using techniques known in the art.

In a preferred embodiment, the angiogenesis proteins are derivative or variant angiogenesis proteins as compared to the wild-type sequence. That is, as outlined more fully below, the derivative angiogenesis peptide will often contain at least one amino acid substitution, deletion or insertion, with amino acid substitutions being particularly preferred. The amino acid substitution, insertion or deletion may occur at any residue within the angiogenesis peptide.

Also included within one embodiment of angiogenesis proteins of the present invention are amino acid sequence variants. These variants typically fall into one or more of three classes: substitutional, insertional or deletional variants. These variants ordinarily are prepared by site specific mutagenesis of nucleotides in the DNA encoding the angiogenesis protein, using cassette or PCR mutagenesis or other techniques well known in the art, to produce DNA encoding the variant, and thereafter expressing the DNA in recombinant cell culture as outlined above. However, variant angiogenesis protein fragments having up to about 100-150 residues may be prepared by in vitro synthesis using established techniques. Amino acid sequence variants are characterized by the predetermined nature of the variation, a feature that sets them apart from naturally occurring allelic or interspecies variation of the angiogenesis protein amino acid sequence. The variants typically exhibit the same qualitative biological activity as the naturally occurring analogue, although variants can also be selected which have modified characteristics as will be more fully outlined below.

While the site or region for introducing an amino acid sequence variation is predetermined, the mutation per se need not be predetermined. For example, in order to optimize the performance of a mutation at a given site, random mutagenesis may be conducted at the target codon or region and the expressed angiogenesis variants screened for the optimal combination of desired activity. Techniques for making substitution mutations at predetermined sites in DNA having a known sequence are well known, for example, M13 primer mutagenesis and PCR mutagenesis. Screening of the mutants is done using assays of angiogenesis protein activities.

Amino acid substitutions are typically of single residues; insertions usually will be on the order of from about 1 to 20 amino acids, although considerably larger

insertions may be tolerated. Deletions range from about 1 to about 20 residues, although in some cases deletions may be much larger.

Substitutions, deletions, insertions or any combination thereof may be used to arrive at a final derivative. Generally these changes are done on a few amino acids to minimize the alteration of the molecule. However, larger changes may be tolerated in certain circumstances. When small alterations in the characteristics of the angiogenesis protein are desired, substitutions are generally made in accordance with the amino acid substitution chart provided in the definition section.

Substantial changes in function or immunological identity are made by selecting substitutions that are less conservative than those provided in the definition of "conservative substitution". For example, substitutions may be made which more significantly affect: the structure of the polypeptide backbone in the area of the alteration, for example the alpha-helical or beta-sheet structure; the charge or hydrophobicity of the molecule at the target site; or the bulk of the side chain. The substitutions which in general are expected to produce the greatest changes in the polypeptide's properties are those in which (a) a hydrophilic residue, *e.g.* seryl or threonyl, is substituted for (or by) a hydrophobic residue, *e.g.* leucyl, isoleucyl, phenylalanyl, valyl or alanyl; (b) a cysteine or proline is substituted for (or by) any other residue; (c) a residue having an electropositive side chain, *e.g.* lysyl, arginyl, or histidyl, is substituted for (or by) an electronegative residue, *e.g.* glutamyl or aspartyl; or (d) a residue having a bulky side chain, *e.g.* phenylalanine, is substituted for (or by) one not having a side chain, *e.g.* glycine.

The variants typically exhibit the same qualitative biological activity and will elicit the same immune response as the naturally-occurring analog, although variants also are selected to modify the characteristics of the angiogenesis proteins as needed. Alternatively, the variant may be designed such that the biological activity of the angiogenesis protein is altered. For example, glycosylation sites may be altered or removed.

Covalent modifications of angiogenesis polypeptides are included within the scope of this invention. One type of covalent modification includes reacting targeted amino acid residues of an angiogenesis polypeptide with an organic derivatizing agent that is capable of reacting with selected side chains or the N-or C-terminal residues of an angiogenesis polypeptide. Derivatization with bifunctional agents is useful, for instance, for crosslinking angiogenesis polypeptides to a water-insoluble support matrix or surface for use in the method for purifying anti-angiogenesis polypeptide antibodies or screening assays, as is more fully described below. Commonly used crosslinking agents include, *e.g.*, 1,1-

bis(diazoacetyl)-2-phenylethane, glutaraldehyde, N-hydroxysuccinimide esters, for example, esters with 4-azidosalicylic acid, homobifunctional imidoesters, including disuccinimidyl esters such as 3,3'-dithiobis(succinimidylpropionate), bifunctional maleimides such as bis-N-maleimido-1,8-octane and agents such as methyl-3-[(p-azidophenyl)dithio]propioimidate.

Other modifications include deamidation of glutaminyl and asparaginyl residues to the corresponding glutamyl and aspartyl residues, respectively, hydroxylation of proline and lysine, phosphorylation of hydroxyl groups of seryl, threonyl or tyrosyl residues, methylation of the γ-amino groups of lysine, arginine, and histidine side chains [T.E. Creighton, Proteins: Structure and Molecular Properties, W.H. Freeman & Co., San Francisco, pp. 79-86 (1983)], acetylation of the N-terminal amine, and amidation of any C-terminal carboxyl group.

Another type of covalent modification of the angiogenesis polypeptide included within the scope of this invention comprises altering the native glycosylation pattern of the polypeptide. "Altering the native glycosylation pattern" is intended for purposes herein to mean deleting one or more carbohydrate moieties found in native sequence angiogenesis polypeptide, and/or adding one or more glycosylation sites that are not present in the native sequence angiogenesis polypeptide. Glycosylation patterns can be altered in many ways. For example the use of different cell types to express angiogenesis-associated sequences can result in different glycosylation patterns.

Addition of glycosylation sites to angiogenesis polypeptides may also be accomplished by altering the amino acid sequence thereof. The alteration may be made, for example, by the addition of, or substitution by, one or more serine or threonine residues to the native sequence angiogenesis polypeptide (for O-linked glycosylation sites). The angiogenesis amino acid sequence may optionally be altered through changes at the DNA level, particularly by mutating the DNA encoding the angiogenesis polypeptide at preselected bases such that codons are generated that will translate into the desired amino acids.

Another means of increasing the number of carbohydrate moieties on the angiogenesis polypeptide is by chemical or enzymatic coupling of glycosides to the polypeptide. Such methods are described in the art, e.g., in WO 87/05330 published 11 September 1987, and in Aplin and Wriston, CRC Crit. Rev. Biochem., pp. 259-306 (1981).

Removal of carbohydrate moieties present on the angiogenesis polypeptide may be accomplished chemically or enzymatically or by mutational substitution of codons encoding for amino acid residues that serve as targets for glycosylation. Chemical

deglycosylation techniques are known in the art and described, for instance, by Hakimuddin, et al., Arch. Biochem. Biophys., 259:52 (1987) and by Edge et al., Anal. Biochem., 118:131 (1981). Enzymatic cleavage of carbohydrate moieties on polypeptides can be achieved by the use of a variety of endo-and exo-glycosidases as described by Thotakura et al., Meth. Enzymol., 138:350 (1987).

Another type of covalent modification of angiogenesis comprises linking the angiogenesis polypeptide to one of a variety of nonproteinaceous polymers, e.g., polyethylene glycol, polypropylene glycol, or polyoxyalkylenes, in the manner set forth in U.S. Patent Nos. 4,640,835; 4,496,689; 4,301,144; 4,670,417; 4,791,192 or 4,179,337.

Angiogenesis polypeptides of the present invention may also be modified in a way to form chimeric molecules comprising an angiogenesis polypeptide fused to another, heterologous polypeptide or amino acid sequence. In one embodiment, such a chimeric molecule comprises a fusion of an angiogenesis polypeptide with a tag polypeptide which provides an epitope to which an anti-tag antibody can selectively bind. The epitope tag is generally placed at the amino-or carboxyl-terminus of the angiogenesis polypeptide. The presence of such epitope-tagged forms of an angiogenesis polypeptide can be detected using an antibody against the tag polypeptide. Also, provision of the epitope tag enables the angiogenesis polypeptide to be readily purified by affinity purification using an anti-tag antibody or another type of affinity matrix that binds to the epitope tag. In an alternative embodiment, the chimeric molecule may comprise a fusion of an angiogenesis polypeptide with an immunoglobulin or a particular region of an immunoglobulin. For a bivalent form of the chimeric molecule, such a fusion could be to the Fc region of an IgG molecule.

Various tag polypeptides and their respective antibodies are well known in the art. Examples include poly-histidine (poly-his) or poly-histidine-glycine (poly-his-gly) tags; HIS6 and metal chelation tags, the flu HA tag polypeptide and its antibody 12CA5 [Field *et al., Mol. Cell. Biol.*, 8:2159-2165 (1988)]; the c-myc tag and the 8F9, 3C7, 6E10, G4, B7 and 9E10 antibodies thereto [Evan *et al., Molecular and Cellular Biology*, 5:3610-3616 (1985)]; and the Herpes Simplex virus glycoprotein D (gD) tag and its antibody [*Paborsky et al., Protein Engineering*, 3(6):547-553 (1990)]. Other tag polypeptides include the Flag-peptide [*Hopp et al., BioTechnology*, 6:1204-1210 (1988)]; the KT3 epitope peptide [Martin *et al., Science*, 255:192-194 (1992)]; tubulin epitope peptide [Skinner *et al., J. Biol. Chem.*, 266:15163-15166 (1991)]; and the T7 gene 10 protein peptide tag [Lutz-Freyermuth *et al., Proc. Natl. Acad. Sci. USA*, 87:6393-6397 (1990)].

Also included with an embodiment of angiogenesis protein are other angiogenesis proteins of the angiogenesis family, and angiogenesis proteins from other organisms, which are cloned and expressed as outlined below. Thus, probe or degenerate polymerase chain reaction (PCR) primer sequences may be used to find other related angiogenesis proteins from humans or other organisms. As will be appreciated by those in the art, particularly useful probe and/or PCR primer sequences include the unique areas of the angiogenesis nucleic acid sequence. As is generally known in the art, preferred PCR primers are from about 15 to about 35 nucleotides in length, with from about 20 to about 30 being preferred, and may contain inosine as needed. The conditions for the PCR reaction are well known in the art (*e.g.*, Innis, PCR Protocols, *supra*).

In addition, as is outlined herein, angiogenesis proteins can be made that are longer than those encoded by the nucleic acids of the figures, *e.g.*, by the elucidation of extended sequences, the addition of epitope or purification tags, the addition of other fusion sequences, etc.

Angiogenesis proteins may also be identified as being encoded by angiogenesis nucleic acids. Thus, angiogenesis proteins are encoded by nucleic acids that will hybridize to the sequences of the sequence listings, or their complements, as outlined herein.

In a preferred embodiment, when the angiogenesis protein is to be used to generate antibodies, *e.g.*, for immunotherapy or immunodiagnosis, the angiogenesis protein should share at least one epitope or determinant with the full length protein. By "epitope" or "determinant" herein is typically meant a portion of a protein which will generate and/or bind an antibody or T-cell receptor in the context of MHC. Thus, in most instances, antibodies made to a smaller angiogenesis protein will be able to bind to the full-length protein, particularly linear epitopes. In a preferred embodiment, the epitope is unique; that is, antibodies generated to a unique epitope show little or no cross-reactivity. In a preferred embodiment, the epitope is selected from a protein sequence set out in Table 2.

Methods of preparing polyclonal antibodies are known to the skilled artisan (*e.g.*, Coligan, *supra*; and Harlow & Lane, *supra*). Polyclonal antibodies can be raised in a mammal, *e.g.*, by one or more injections of an immunizing agent and, if desired, an adjuvant. Typically, the immunizing agent and/or adjuvant will be injected in the mammal by multiple subcutaneous or intraperitoneal injections. The immunizing agent may include a protein encoded by a nucleic acid of the figures or fragment thereof or a fusion protein thereof. It may be useful to conjugate the immunizing agent to a protein known to be immunogenic in

the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. Examples of adjuvants which may be employed include Freund's complete adjuvant and MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate). The immunization protocol may be selected by one skilled in the art without undue experimentation.

The antibodies may, alternatively, be monoclonal antibodies. Monoclonal antibodies may be prepared using hybridoma methods, such as those described by Kohler and Milstein, Nature, 256:495 (1975). In a hybridoma method, a mouse, hamster, or other appropriate host animal, is typically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes may be immunized in vitro. The immunizing agent will typically include a polypeptide encoded by a nucleic acid of Table 1, or fragment thereof, or a fusion protein thereof. Generally, either peripheral blood lymphocytes ("PBLs") are used if cells of human origin are desired, or spleen cells or lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell [Goding, Monoclonal Antibodies: Principles and Practice, Academic Press, (1986) pp. 59-103]. Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells may be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

In one embodiment, the antibodies are bispecific antibodies. Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens or that have binding specificities for two epitopes on the same antigen. In one embodiment, one of the binding specificities is for a protein encoded by a nucleic acid Table 1 or a fragment thereof, the other one is for any other antigen, and preferably for a cell-surface protein or receptor or receptor subunit, preferably one that is tumor specific. Alternatively, tetramer-type technology may create multivalent reagents.

In a preferred embodiment, the antibodies to angiogenesis protein are capable of reducing or eliminating a biological function of an angiogenesis protein, as is described below. That is, the addition of anti-angiogenesis protein antibodies (either polyclonal or preferably monoclonal) to angiogenic tissue (or cells containing angiogenesis) may reduce or eliminate the angiogenesis activity. Generally, at least a 25% decrease in activity is preferred, with at least about 50% being particularly preferred and about a 95-100% decrease being especially preferred.

In a preferred embodiment the antibodies to the angiogenesis proteins are humanized antibodies (*e.g.*, Xenerex Biosciences, Mederex, Inc., Abgenix, Inc., Protein Design Labs,Inc.) Humanized forms of non-human (e.g., murine) antibodies are chimeric molecules of immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')2 or other antigen-binding subsequences of antibodies) which contain minimal sequence derived from non-human immunoglobulin. Humanized antibodies include human immunoglobulins (recipient antibody) in which residues form a complementary determining region (CDR) of the recipient are replaced by residues from a CDR of a non-human species (donor antibody) such as mouse, rat or rabbit having the desired specificity, affinity and capacity. In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies may also comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. In general, a humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the framework (FR) regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin [Jones et al., Nature, 321:522-525 (1986); Riechmann et al., Nature, 332:323-329 (1988); and Presta, Curr. Op. Struct. Biol., 2:593-596 (1992)].

Methods for humanizing non-human antibodies are well known in the art. Generally, a humanized antibody has one or more amino acid residues introduced into it from a source which is non-human. These non-human amino acid residues are often referred to as import residues, which are typically taken from an import variable domain. Humanization can be essentially performed following the method of Winter and co-workers [Jones et al., Nature, 321:522-525 (1986); Riechmann et al., Nature, 332:323-327 (1988); Verhoeyen et al., Science, 239:1534-1536 (1988)], by substituting rodent CDRs or CDR sequences for the

corresponding sequences of a human antibody. Accordingly, such humanized antibodies are chimeric antibodies (U.S. Patent No. 4,816,567), wherein substantially less than an intact human variable domain has been substituted by the corresponding sequence from a non-human species. In practice, humanized antibodies are typically human antibodies in which some CDR residues and possibly some FR residues are substituted by residues from analogous sites in rodent antibodies.

Human antibodies can also be produced using various techniques known in the art, including phage display libraries [Hoogenboom and Winter, J. Mol. Biol., 227:381 (1991); Marks et al., J. Mol. Biol., 222:581 (1991)]. The techniques of Cole et al. and Boerner et al. are also available for the preparation of human monoclonal antibodies (Cole et al., Monoclonal Antibodies and Cancer Therapy, Alan R. Liss, p. 77 (1985) and Boerner et al., J. Immunol., 147(1):86-95 (1991)]. Similarly, human antibodies can be made by introducing of human immunoglobulin loci into transgenic animals, e.g., mice in which the endogenous immunoglobulin genes have been partially or completely inactivated. Upon challenge, human antibody production is observed, which closely resembles that seen in humans in all respects, including gene rearrangement, assembly, and antibody repertoire. This approach is described, for example, in U.S. Patent Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in the following scientific publications: Marks et al., Bio/Technology 10, 779-783 (1992); Lonberg et al., Nature 368 856-859 (1994); Morrison, Nature 368, 812-13 (1994); Fishwild et al., Nature Biotechnology 14, 845-51 (1996); Neuberger, Nature Biotechnology 14, 826 (1996); Lonberg and Huszar, Intern. Rev. Immunol. 13 65-93 (1995).

By immunotherapy is meant treatment of angiogenesis with an antibody raised against angiogenesis proteins. As used herein, immunotherapy can be passive or active. Passive immunotherapy as defined herein is the passive transfer of antibody to a recipient (patient). Active immunization is the induction of antibody and/or T-cell responses in a recipient (patient). Induction of an immune response is the result of providing the recipient with an antigen to which antibodies are raised. As appreciated by one of ordinary skill in the art, the antigen may be provided by injecting a polypeptide against which antibodies are desired to be raised into a recipient, or contacting the recipient with a nucleic acid capable of expressing the antigen and under conditions for expression of the antigen, leading to an immune response.

In a preferred embodiment the angiogenesis proteins against which antibodies are raised are secreted proteins as described above. Without being bound by theory,

antibodies used for treatment, bind and prevent the secreted protein from binding to its receptor, thereby inactivating the secreted angiogenesis protein.

In another preferred embodiment, the angiogenesis protein to which antibodies are raised is a transmembrane protein. Without being bound by theory, antibodies used for treatment, bind the extracellular domain of the angiogenesis protein and prevent it from binding to other proteins, such as circulating ligands or cell-associated molecules. The antibody may cause down-regulation of the transmembrane angiogenesis protein. As will be appreciated by one of ordinary skill in the art, the antibody may be a competitive, non-competitive or uncompetitive inhibitor of protein binding to the extracellular domain of the angiogenesis protein. The antibody is also an antagonist of the angiogenesis protein. Further, the antibody prevents activation of the transmembrane angiogenesis protein. In one aspect, when the antibody prevents the binding of other molecules to the angiogenesis protein, the antibody prevents growth of the cell. The antibody may also be used to target or sensitize the cell to cytotoxic agents, including, but not limited to TNF-α, TNF-β, IL-1, INF-γ and IL-2, or chemotherapeutic agents including 5FU, vinblastine, actinomycin D, cisplatin, methotrexate, and the like. In some instances the antibody belongs to a sub-type that activates serum complement when complexed with the transmembrane protein thereby mediating cytotoxicity or antigen-dependent cytotoxicity (ADCC). Thus, angiogenesis is treated by administering to a patient antibodies directed against the transmembrane angiogenesis protein. Antibody-labeling may activate a co-toxin, localize a toxin payload, or otherwise provide means to locally ablate cells.

In another preferred embodiment, the antibody is conjugated to an effector moiety. The effector moiety can be any number of molecules, including labelling moieties such as radioactive labels or fluorescent labels, or can be a therapeutic moiety. In one aspect the therapeutic moiety is a small molecule that modulates the activity of the angiogenesis protein. In another aspect the therapeutic moiety modulates the activity of molecules associated with or in close proximity to the angiogenesis protein. The therapeutic moiety may inhibit enzymatic activity such as protease or collagenase activity associated with angiogenesis.

In a preferred embodiment, the therapeutic moiety can also be a cytotoxic agent. In this method, targeting the cytotoxic agent to angiogenesis tissue or cells, results in a reduction in the number of afflicted cells, thereby reducing symptoms associated with angiogenesis. Cytotoxic agents are numerous and varied and include, but are not limited to,

cytotoxic drugs or toxins or active fragments of such toxins. Suitable toxins and their corresponding fragments include diphtheria A chain, exotoxin A chain, ricin A chain, abrin A chain, curcin, crotin, phenomycin, enomycin and the like. Cytotoxic agents also include radiochemicals made by conjugating radioisotopes to antibodies raised against angiogenesis proteins, or binding of a radionuclide to a chelating agent that has been covalently attached to the antibody. Targeting the therapeutic moiety to transmembrane angiogenesis proteins not only serves to increase the local concentration of therapeutic moiety in the angiogenesis afflicted area, but also serves to reduce deleterious side effects that may be associated with the therapeutic moiety.

In another preferred embodiment, the angiogenesis protein against which the antibodies are raised is an intracellular protein. In this case, the antibody may be conjugated to a protein which facilitates entry into the cell. In one case, the antibody enters the cell by endocytosis. In another embodiment, a nucleic acid encoding the antibody is administered to the individual or cell. Moreover, wherein the angiogenesis protein can be targeted within a cell, i.e., the nucleus, an antibody thereto contains a signal for that target localization, i.e., a nuclear localization signal.

The angiogenesis antibodies of the invention specifically bind to angiogenesis proteins. By "specifically bind" herein is meant that the antibodies bind to the protein with a K_d of at least about 0.1 mM, more usually at least about 1 μM, preferably at least about 0.1 μM or better, and most preferably, 0.01 μM or better. Selectivity of binding is also important.

In a preferred embodiment, the angiogenesis protein is purified or isolated after expression. Angiogenesis proteins may be isolated or purified in a variety of ways known to those skilled in the art depending on what other components are present in the sample. Standard purification methods include electrophoretic, molecular, immunological and chromatographic techniques, including ion exchange, hydrophobic, affinity, and reverse-phase HPLC chromatography, and chromatofocusing. For example, the angiogenesis protein may be purified using a standard anti-angiogenesis protein antibody column. Ultrafiltration and diafiltration techniques, in conjunction with protein concentration, are also useful. For general guidance in suitable purification techniques, see Scopes, R., Protein Purification, Springer-Verlag, NY (1982). The degree of purification necessary will vary depending on the use of the angiogenesis protein. In some instances no purification will be necessary.

Once expressed and purified if necessary, the angiogenesis proteins and nucleic acids are useful in a number of applications. They may be used as immunoselection reagents, as vaccine reagents, as screening agents, etc.

Detection of angiogenesis sequence for diagnostic and therapeutic applications

In one aspect, the RNAexpression levels of genes are determined for different cellular states in the angiogenesis phenotype. Expression levels of genes in normal tissue (*i.e.*, not undergoing angiogenesis) and in angiogenesis tissue (and in some cases, for varying severities of angiogenesis that relate to prognosis, as outlined below) are evaluated to provide expression profiles. An expression profile of a particular cell state or point of development is essentially a "fingerprint" of the state. While two states may have any particular gene similarly expressed, the evaluation of a number of genes simultaneously allows the generation of a gene expression profile that is reflective of the state of the cell. By comparing expression profiles of cells in different states, information regarding which genes are important (including both up- and down-regulation of genes) in each of these states is obtained. Then, diagnosis may be performed or confirmed to determine whether a tissue sample has the gene expression profile of normal or angiogenesic tissue. This will provide for molecular diagnosis of related conditions.

"Differential expression," or grammatical equivalents as used herein, refers to qualitative or quantitative differences in the temporal and/or cellular gene expression patterns within and among cells and tissue. Thus, a differentially expressed gene can qualitatively have its expression altered, including an activation or inactivation, in, *e.g.*, normal versus angiogenic tissue. Genes may be turned on or turned off in a particular state, relative to another state thus permitting comparison of two or more statese. A qualitatively regulated gene will exhibit an expression pattern within a state or cell type which is detectable by standard techniques. Some genes will be expressed in one state or cell type, but not in both. Alternatively, the difference in expression may be quantitative, *e.g.*, in that expression is increased or decreased; *i.e.*, gene expression is either upregulated, resulting in an increased amount of transcript, or downregulated, resulting in a decreased amount of transcript. The degree to which expression differs need only be large enough to quantify via standard characterization techniques as outlined below, such as by use of Affymetrix GeneChip™ expression arrays, Lockhart, Nature Biotechnology, 14:1675-1680 (1996), hereby expressly incorporated by reference. Other techniques include, but are not limited to, quantitative reverse transcriptase PCR, Northern analysis and RNase protection. As outlined

above, preferably the change in expression (*i.e.*, upregulation or downregulation) is at least about 50%, more preferably at least about 100%, more preferably at least about 150%, more preferably at least about 200%, with from 300 to at least 1000% being especially preferred.

Evaluation may be at the gene transcript, or the protein level. The amount of gene expression may be monitored using nucleic acid probes to the DNA or RNA equivalent of the gene transcript, and the quantification of gene expression levels, or, alternatively, the final gene product itself (protein) can be monitored, *e.g.*, with antibodies to the angiogenesis protein and standard immunoassays (ELISAs, etc.) or other techniques, including mass spectroscopy assays, 2D gel electrophoresis assays, etc. Proteins corresponding to angiogenesis genes, *i.e.*, those identified as being important in an angiogenesis phenotype, can be evaluated in an angiogenesis diagnostic test.

In a preferred embodiment, gene expression monitoring is performed simultaneously on a number of genes. Multiple protein expression monitoring can be performed as well. Similarly, these assays may be performed on an individual basis as well.

In this embodiment, the angiogenesis nucleic acid probes are attached to biochips as outlined herein for the detection and quantification of angiogenesis sequences in a particular cell. The assays are further described below in the example. PCR techniques can be used to provide greater sensitivity.

In a preferred embodiment nucleic acids encoding the angiogenesis protein are detected. Although DNA or RNA encoding the angiogenesis protein may be detected, of particular interest are methods wherein an mRNA encoding an angiogenesis protein is detected. Probes to detect mRNA can be a nucleotide/deoxynucleotide probe that is complementary to and hybridizes with the mRNA and includes, but is not limited to, oligonucleotides, cDNA or RNA. Probes also should contain a detectable label, as defined herein. In one method the mRNA is detected after immobilizing the nucleic acid to be examined on a solid support such as nylon membranes and hybridizing the probe with the sample. Following washing to remove the non-specifically bound probe, the label is detected. In another method detection of the mRNA is performed in situ. In this method permeabilized cells or tissue samples are contacted with a detectably labeled nucleic acid probe for sufficient time to allow the probe to hybridize with the target mRNA. Following washing to remove the non-specifically bound probe, the label is detected. For example a digoxygenin labeled riboprobe (RNA probe) that is complementary to the mRNA encoding an angiogenesis protein is detected by binding the digoxygenin with an anti-digoxygenin

secondary antibody and developed with nitro blue tetrazolium and 5-bromo-4-chloro-3-indoyl phosphate.

In a preferred embodiment, various proteins from the three classes of proteins as described herein (secreted, transmembrane or intracellular proteins) are used in diagnostic assays. The angiogenesis proteins, antibodies, nucleic acids, modified proteins and cells containing angiogenesis sequences are used in diagnostic assays. This can be performed on an individual gene or corresponding polypeptide level. In a preferred embodiment, the expression profiles are used, preferably in conjunction with high throughput screening techniques to allow monitoring for expression profile genes and/or corresponding polypeptides.

As described and defined herein, angiogenesis proteins, including intracellular, transmembrane or secreted proteins, find use as markers of angiogenesis. Detection of these proteins in putative angiogenesis tissue allows for detection or diagnosis of angiogenesis. In one embodiment, antibodies are used to detect angiogenesis proteins. A preferred method separates proteins from a sample by electrophoresis on a gel (typically a denaturing and reducing protein gel, but may be another type of gel, including isoelectric focusing gels and the like). Following separation of proteins, the angiogenesis protein is detected, *e.g.*, by immunoblotting with antibodies raised against the angiogenesis protein. Methods of immunoblotting are well known to those of ordinary skill in the art.

In another preferred method, antibodies to the angiogenesis protein find use in *in situ* imaging techniques, *e.g.*, in histology (*e.g.*, *Methods in Cell Biology: Antibodies in Cell Biology*, volume 37 (Asai, ed. 1993)). In this method cells are contacted with from one to many antibodies to the angiogenesis protein(s). Following washing to remove non-specific antibody binding, the presence of the antibody or antibodies is detected. In one embodiment the antibody is detected by incubating with a secondary antibody that contains a detectable label. In another method the primary antibody to the angiogenesis protein(s) contains a detectable label, for example an enzyme marker that can act on a substrate. In another preferred embodiment each one of multiple primary antibodies contains a distinct and detectable label. This method finds particular use in simultaneous screening for a plurality of angiogenesis proteins. As will be appreciated by one of ordinary skill in the art, many other histological imaging techniques are alsoprovided by the invention.

In a preferred embodiment the label is detected in a fluorometer which has the ability to detect and distinguish emissions of different wavelengths. In addition, a fluorescence activated cell sorter (FACS) can be used in the method.

In another preferred embodiment, antibodies find use in diagnosing angiogenesis from blood samples. As previously described, certain angiogenesis proteins are secreted/circulating molecules. Blood samples, therefore, are useful as samples to be probed or tested for the presence of secreted angiogenesis proteins. Antibodies can be used to detect an angiogenesis protein by previously described immunoassay techniques including ELISA, immunoblotting (Western blotting), immunoprecipitation, BIACORE technology and the like. Conversely, the presence of antibodies may indicate an immune response against an endogenous angiogenesis protein.

In a preferred embodiment, *in situ* hybridization of labeled angiogenesis nucleic acid probes to tissue arrays is done. For example, arrays of tissue samples, including angiogenesis tissue and/or normal tissue, are made. *In situ* hybridization (*see, e.g.*, Ausubel, *supra*) is then performed. When comparing the fingerprints between an individual and a standard, the skilled artisan can make a diagnosis, a prognosis, or a prediction based on the findings. It is further understood that the genes which indicate the diagnosis may differ from those which indicate the prognosis and molecular profiling of the condition of the cells may lead to distinctions between responsive or refractory conditions or may be predictive of outcomes.

In a preferred embodiment, the angiogenesis proteins, antibodies, nucleic acids, modified proteins and cells containing angiogenesis sequences are used in prognosis assays. As above, gene expression profiles can be generated that correlate to angiogenesis severity, in terms of long term prognosis. Again, this may be done on either a protein or gene level, with the use of genes being preferred. As above, angiogenesis probes may be attached to biochips for the detection and quantification of angiogenesis sequences in a tissue or patient. The assays proceed as outlined above for diagnosis. PCR method may provide more sensitive and accurate quantification.

In a preferred embodiment members of the three classes of proteins as described herein are used in drug screening assays. The angiogenesis proteins, antibodies, nucleic acids, modified proteins and cells containing angiogenesis sequences are used in drug screening assays or by evaluating the effect of drug candidates on a "gene expression profile" or expression profile of polypeptides. In a preferred embodiment, the expression profiles are used, preferably in conjunction with high throughput screening techniques to allow monitoring for expression profile genes after treatment with a candidate agent (e.g., Zlokarnik, et al., Science 279, 84-8 (1998); Heid, *Genome Res* 6:986-94, 1996).

In a preferred embodiment, the angiogenesis proteins, antibodies, nucleic acids, modified proteins and cells containing the native or modified angiogenesis proteins are used in screening assays. That is, the present invention provides novel methods for screening for compositions which modulate the angiogenesis phenotype or an identified physiological function of an angiogenesis protein. As above, this can be done on an individual gene level or by evaluating the effect of drug candidates on a "gene expression profile". In a preferred embodiment, the expression profiles are used, preferably in conjunction with high throughput screening techniques to allow monitoring for expression profile genes after treatment with a candidate agent, see Zlokarnik, *supra*.

Having identified the differentially expressed genes herein, a variety of assays may be executed. In a preferred embodiment, assays may be run on an individual gene or protein level. That is, having identified a particular gene as up regulated in angiogenesis, test compounds can be screened for the ability to modulate gene expression or for binding to the angiogenic protein. "Modulation" thus includes both an increase and a decrease in gene expression. The preferred amount of modulation will depend on the original change of the gene expression in normal versus tissue undergoing angiogenesis, with changes of at least 10%, preferably 50%, more preferably 100-300%, and in some embodiments 300-1000% or greater. Thus, if a gene exhibits a 4-fold increase in angiogenic tissue compared to normal tissue, a decrease of about four-fold is often desired; similarly, a 10-fold decrease in angiogenic tissue compared to normal tissue often provides a target value of a 10-fold increase in expression to be induced by the test compound.

The amount of gene expression may be monitored using nucleic acid probes and the quantification of gene expression levels, or, alternatively, the gene product itself can be monitored, *e.g.*, through the use of antibodies to the angiogenesis protein and standard immunoassays. Proteomics and separation techniques may also allow quantification of expression.

In a preferred embodiment, gene expression or protein monitoring of a number of entitites, *i.e.*, an expression profile, is monitored simultaneously. Such profiles will typically invove a plurality of those entitites described herein..

In this embodiment, the angiogenesis nucleic acid probes are attached to biochips as outlined herein for the detection and quantification of angiogenesis sequences in a particular cell. Alternatively, PCR may be used. Thus, a series, e.g., of microtiter plate, may be used with dispensed primers in desired wells. A PCR reaction can then be performed and analyzed for each well.

Modulators of angiogenesis

Expression monitoring can be performed to identify compounds that modify the expression of one or more angiogenesis-associated sequences, *e.g.*, a polynucleotide sequence set out in Table 1. Generally, in a preferred embodiment, a test modulator is added to the cells prior to analysis. Moreover, screens are also provided to identify agents that modulate angiogenesis, modulate angiogenesis proteins, bind to an angiogenesis protein, or interfere with the binding of an angiogenesis protein and an antibody or other binding partner.

The term "test compound" or "drug candidate" or "modulator" or grammatical equivalents as used herein describes any molecule, *e.g.*, protein, oligopeptide, small organic molecule, polysaccharide, polynucleotide, *etc.*, to be tested for the capacity to directly or indirectly alter the angiogenesis phenotype or the expression of an angiogenesis sequence, *e.g.*, a nucleic acid or protein sequence. In preferred embodiments, modulators alter expression profiles, or expression profile nucleic acids or proteins provided herein. In one embodiment, the modulator suppresses an angiogenesis phenotype, for example to a normal tissue fingerprint. In another embodiment, a modulator induced an angiogenesis phenotype. Generally, a plurality of assay mixtures are run in parallel with different agent concentrations to obtain a differential response to the various concentrations. Typically, one of these concentrations serves as a negative control, *i.e.*, at zero concentration or below the level of detection.

In one aspect, a modulator will neutralize the effect of an angiogenesis protein. By "neutralize" is meant that activity of a protein is inhibited or blocked and thereby has substantially no effect on a cell.

In certain embodiments, combinatorial libraries of potential modulators will be screened for an ability to bind to an angiogenesis polypeptide or to modulate activity. Conventionally, new chemical entities with useful properties are generated by identifying a chemical compound (called a "lead compound") with some desirable property or activity, *e.g.*, inhibiting activity, creating variants of the lead compound, and evaluating the property and activity of those variant compounds. Often, high throughput screening (HTS) methods are employed for such an analysis.

In one preferred embodiment, high throughput screening methods involve providing a library containing a large number of potential therapeutic compounds (candidate compounds). Such "combinatorial chemical libraries" are then screened in one or more

assays to identify those library members (particular chemical species or subclasses) that display a desired characteristic activity. The compounds thus identified can serve as conventional "lead compounds" or can themselves be used as potential or actual therapeutics.

A combinatorial chemical library is a collection of diverse chemical compounds generated by either chemical synthesis or biological synthesis by combining a number of chemical "building blocks" such as reagents. For example, a linear combinatorial chemical library, such as a polypeptide (*e.g.*, mutein) library, is formed by combining a set of chemical building blocks called amino acids in every possible way for a given compound length (*i.e.*, the number of amino acids in a polypeptide compound). Millions of chemical compounds can be synthesized through such combinatorial mixing of chemical building blocks (Gallop *et al.* (1994) *J. Med. Chem.* 37(9): 1233-1251).

Preparation and screening of combinatorial chemical libraries is well known to those of skill in the art. Such combinatorial chemical libraries include, but are not limited to, peptide libraries (*see, e.g.*, U.S. Patent No. 5,010,175, Furka (1991) *Int. J. Pept. Prot. Res.*, 37: 487-493, Houghton *et al.* (1991) *Nature*, 354: 84-88), peptoids (PCT Publication No WO 91/19735, 26 Dec. 1991), encoded peptides (PCT Publication WO 93/20242, 14 Oct. 1993), random bio-oligomers (PCT Publication WO 92/00091, 9 Jan. 1992), benzodiazepines (U.S. Pat. No. 5,288,514), diversomers such as hydantoins, benzodiazepines and dipeptides (Hobbs *et al.*, (1993) *Proc. Nat. Acad. Sci. USA* 90: 6909-6913), vinylogous polypeptides (Hagihara *et al.* (1992) *J. Amer. Chem. Soc.* 114: 6568), nonpeptidal peptidomimetics with a Beta-D-Glucose scaffolding (Hirschmann *et al.*, (1992) *J. Amer. Chem. Soc.* 114: 9217-9218), analogous organic syntheses of small compound libraries (Chen *et al.* (1994) *J. Amer. Chem. Soc.* 116: 2661), oligocarbamates (Cho, et al., (1993) *Science* 261:1303), and/or peptidyl phosphonates (Campbell *et al.*, (1994) *J. Org. Chem.* 59: 658). *See, generally,* Gordon *et al.*, (1994) *J. Med. Chem.* 37:1385, nucleic acid libraries (*see, e.g.*, Strategene, Corp.), peptide nucleic acid libraries (*see, e.g.*, U.S. Patent 5,539,083), antibody libraries (*see, e.g.*, Vaughn *et al.* (1996) *Nature Biotechnology*, 14(3): 309-314), and PCT/US96/10287), carbohydrate libraries (*see, e.g.*, Liang *et al.*, (1996) *Science*, 274: 1520-1522, and U.S. Patent No. 5,593,853), and small organic molecule libraries (*see, e.g.*, benzodiazepines, Baum (1993) C&EN, Jan 18, page 33; isoprenoids, U.S. Patent No. 5,569,588; thiazolidinones and metathiazanones, U.S. Patent No. 5,549,974; pyrrolidines, U.S. Patent Nos. 5,525,735 and 5,519,134; morpholino compounds, U.S. Patent No. 5,506,337; benzodiazepines, U.S. Patent No. 5,288,514; and the like).

Devices for the preparation of combinatorial libraries are commercially available (*see, e.g.*, 357 MPS, 390 MPS, Advanced Chem Tech, Louisville KY, Symphony, Rainin, Woburn, MA, 433A Applied Biosystems, Foster City, CA, 9050 Plus, Millipore, Bedford, MA).

A number of well known robotic systems have also been developed for solution phase chemistries. These systems include automated workstations like the automated synthesis apparatus developed by Takeda Chemical Industries, LTD. (Osaka, Japan) and many robotic systems utilizing robotic arms (Zymate II, Zymark Corporation, Hopkinton, Mass.; Orca, Hewlett-Packard, Palo Alto, Calif.), which mimic the manual synthetic operations performed by a chemist. Any of the above devices are suitable for use with the present invention. The nature and implementation of modifications to these devices (if any) so that they can operate as discussed herein will be apparent to persons skilled in the relevant art. In addition, numerous combinatorial libraries are themselves commercially available (*see, e.g.*, ComGenex, Princeton, N.J., Asinex, Moscow, Ru, Tripos, Inc., St. Louis, MO, ChemStar, Ltd, Moscow, RU, 3D Pharmaceuticals, Exton, PA, Martek Biosciences, Columbia, MD, *etc.*).

The assays to identify modulators are amenable to high throughput screening. Preferred assays thus detect enhancement or inhibition of angiogenesis gene transcription, inhibition or enhancement of polypeptide expression, and inhibition or enhancement of polypeptide activity.

High throughput assays for the presence, absence, quantification, or other properties of particular nucleic acids or protein products are well known to those of skill in the art. Similarly, binding assays and reporter gene assays are similarly well known. Thus, for example, U.S. Patent No. 5,559,410 discloses high throughput screening methods for proteins, U.S. Patent No. 5,585,639 discloses high throughput screening methods for nucleic acid binding (*i.e.*, in arrays), while U.S. Patent Nos. 5,576,220 and 5,541,061 disclose high throughput methods of screening for ligand/antibody binding.

In addition, high throughput screening systems are commercially available (*see, e.g.*, Zymark Corp., Hopkinton, MA; Air Technical Industries, Mentor, OH; Beckman Instruments, Inc. Fullerton, CA; Precision Systems, Inc., Natick, MA, *etc.*). These systems typically automate entire procedures, including all sample and reagent pipetting, liquid dispensing, timed incubations, and final readings of the microplate in detector(s) appropriate for the assay. These configurable systems provide high throughput and rapid start up as well as a high degree of flexibility and customization. The manufacturers of such systems provide

detailed protocols for various high throughput systems. Thus, for example, Zymark Corp. provides technical bulletins describing screening systems for detecting the modulation of gene transcription, ligand binding, and the like.

In one embodiment, modulators are proteins, often naturally occurring proteins or fragments of naturally occurring proteins. Thus, *e.g.*, cellular extracts containing proteins, or random or directed digests of proteinaceous cellular extracts, may be used. In this way libraries of proteins may be made for screening in the methods of the invention. Particularly preferred in this embodiment are libraries of bacterial, fungal, viral, and mammalian proteins, with the latter being preferred, and human proteins being especially preferred. Paticularly useful test compound will be directed to the class of proteins to which the target belongs, *e.g.*, substrates for enzymes or ligands and receptors.

In a preferred embodiment, modulators are peptides of from about 5 to about 30 amino acids, with from about 5 to about 20 amino acids being preferred, and from about 7 to about 15 being particularly preferred. The peptides may be digests of naturally occurring proteins as is outlined above, random peptides, or "biased" random peptides. By "randomized" or grammatical equivalents herein is meant that each nucleic acid and peptide consists of essentially random nucleotides and amino acids, respectively. Since generally these random peptides (or nucleic acids, discussed below) are chemically synthesized, they may incorporate any nucleotide or amino acid at any position. The synthetic process can be designed to generate randomized proteins or nucleic acids, to allow the formation of all or most of the possible combinations over the length of the sequence, thus forming a library of randomized candidate bioactive proteinaceous agents.

In one embodiment, the library is fully randomized, with no sequence preferences or constants at any position. In a preferred embodiment, the library is biased. That is, some positions within the sequence are either held constant, or are selected from a limited number of possibilities. For example, in a preferred embodiment, the nucleotides or amino acid residues are randomized within a defined class, for example, of hydrophobic amino acids, hydrophilic residues, sterically biased (either small or large) residues, towards the creation of nucleic acid binding domains, the creation of cysteines, for cross-linking, prolines for SH-3 domains, serines, threonines, tyrosines or histidines for phosphorylation sites, etc., or to purines, etc.

Modulators of angiogenesis can also be nucleic acids, as defined above.

As described above generally for proteins, nucleic acid modulating agents may be naturally occurring nucleic acids, random nucleic acids, or "biased" random nucleic acids.

For example, digests of procaryotic or eucaryotic genomes may be used as is outlined above for proteins.

In a preferred embodiment, the candidate compounds are organic chemical moieties, a wide variety of which are available in the literature.

After the candidate agent has been added and the cells allowed to incubate for some period of time, the sample containing a target sequence to be analyzed is added to the biochip. If required, the target sequence is prepared using known techniques. For example, the sample may be treated to lyse the cells, using known lysis buffers, electroporation, etc., with purification and/or amplification such as PCR performed as appropriate. For example, an *in vitro* transcription with labels covalently attached to the nucleotides is performed. Generally, the nucleic acids are labeled with biotin-FITC or PE, or with cy3 or cy5.

In a preferred embodiment, the target sequence is labeled with, for example, a fluorescent, a chemiluminescent, a chemical, or a radioactive signal, to provide a means of detecting the target sequence's specific binding to a probe. The label also can be an enzyme, such as, alkaline phosphatase or horseradish peroxidase, which when provided with an appropriate substrate produces a product that can be detected. Alternatively, the label can be a labeled compound or small molecule, such as an enzyme inhibitor, that binds but is not catalyzed or altered by the enzyme. The label also can be a moiety or compound, such as, an epitope tag or biotin which specifically binds to streptavidin. For the example of biotin, the streptavidin is labeled as described above, thereby, providing a detectable signal for the bound target sequence. Unbound labeled streptavidin is typically removed prior to analysis.

As will be appreciated by those in the art, these assays can be direct hybridization assays or can comprise "sandwich assays", which include the use of multiple probes, as is generally outlined in U.S. Patent Nos. 5,681,702, 5,597,909, 5,545,730, 5,594,117, 5,591,584, 5,571,670, 5,580,731, 5,571,670, 5,591,584, 5,624,802, 5,635,352, 5,594,118, 5,359,100, 5,124,246 and 5,681,697, all of which are hereby incorporated by reference. In this embodiment, in general, the target nucleic acid is prepared as outlined above, and then added to the biochip comprising a plurality of nucleic acid probes, under conditions that allow the formation of a hybridization complex.

A variety of hybridization conditions may be used in the present invention, including high, moderate and low stringency conditions as outlined above. The assays are generally run under stringency conditions which allows formation of the label probe hybridization complex only in the presence of target. Stringency can be controlled by altering a step parameter that is a thermodynamic variable, including, but not limited to,

temperature, formamide concentration, salt concentration, chaotropic salt concentration pH, organic solvent concentration, etc.

These parameters may also be used to control non-specific binding, as is generally outlined in U.S. Patent No. 5,681,697. Thus it may be desirable to perform certain steps at higher stringency conditions to reduce non-specific binding.

The reactions outlined herein may be accomplished in a variety of ways. Components of the reaction may be added simultaneously, or sequentially, in different orders, with preferred embodiments outlined below. In addition, the reaction may include a variety of other reagents. These include salts, buffers, neutral proteins, *e.g.* albumin, detergents, *etc.* which may be used to facilitate optimal hybridization and detection, and/or reduce non-specific or background interactions. Reagents that otherwise improve the efficiency of the assay, such as protease inhibitors, nuclease inhibitors, anti-microbial agents, *etc.*, may also be used as appropriate, depending on the sample preparation methods and purity of the target.

The assay data are analyzed to determine the expression levels, and changes in expression levels as between states, of individual genes, forming a gene expression profile.

Screens are performed to identify modulators of the angiogenesis phenotype. In one embodiment, screening is performed to identify modulators that can induce or suppress a particular expression profile, thus preferably generating the associated phenotype. In another embodiment, *e.g.*, for diagnostic applications, having identified differentially expressed genes important in a particular state, screens can be performed to identify modulators that alter expression of individual genes. In an another embodiment, screening is performed to identify modulators that alter a biological function of the expression product of a differentially expressed gene. Again, having identified the importance of a gene in a particular state, screens are performed to identify agents that bind and/or modulate the biological activity of the gene product.

In addition screens can be done for genes that are induced in response to a candidate agent. After identifying a modulator based upon its ability to suppress an angiogenesis expression pattern leading to a normal expression pattern, or to modulate a single angiogenesis gene expression profile so as to mimic the expression of the gene from normal tissue, a screen as described above can be performed to identify genes that are specifically modulated in response to the agent. Comparing expression profiles between normal tissue and agent treated angiogenesis tissue reveals genes that are not expressed in normal tissue or angiogenesis tissue, but are expressed in agent treated tissue. These agent-specific sequences can be identified and used by methods described herein for angiogenesis

genes or proteins. In particular these sequences and the proteins they encode find use in marking or identifying agent treated cells. In addition, antibodies can be raised against the agent induced proteins and used to target novel therapeutics to the treated angiogenesis tissue sample.

Thus, in one embodiment, a test compound is administered to a population of angiogenic cells, that have an associated angiogenesis expression profile. By "administration" or "contacting" herein is meant that the candidate agent is added to the cells in such a manner as to allow the agent to act upon the cell, whether by uptake and intracellular action, or by action at the cell surface. In some embodiments, nucleic acid encoding a proteinaceous candidate agent (*i.e.*, a peptide) may be put into a viral construct such as an adenoviral or retroviral construct, and added to the cell, such that expression of the peptide agent is accomplished, *e.g.*, PCT US97/01019. Regulatable gene therapy systems can also be used.

Once the test compound has been administered to the cells, the cells can be washed if desired and are allowed to incubate under preferably physiological conditions for some period of time. The cells are then harvested and a new gene expression profile is generated, as outlined herein.

Thus, for example, angiogenesis tissue may be screened for agents that modulate, *e.g.*, induce or suppress the angiogenesis phenotype. A change in at least one gene, preferably many, of the expression profile indicates that the agent has an effect on angiogenesis activity. By defining such a signature for the angiogenesis phenotype, screens for new drugs that alter the phenotype can be devised. With this approach, the drug target need not be known and need not be represented in the original expression screening platform, nor does the level of transcript for the target protein need to change.

Measure of angiogenesis polypeptide activity, or of angiogenesis or the angiogenic phenotype can be performed using a variety of assays. For example, the effects of the test compounds upon the function of the anagiogenesis polypeptides can be measured by examining parameters described above. A suitable physiological change that affects activity can be used to assess the influence of a test compound on the polypeptides of this invention. When the functional consequences are determined using intact cells or animals, one can also measure a variety of effects such as, in the case of angiogenesis associated with tumors, tumor growth, neovascularization, hormone release, transcriptional changes to both known and uncharacterized genetic markers (*e.g.*, northern blots), changes in cell metabolism such as cell growth or pH changes, and changes in intracellular second messengers such as cGMP. In

the assays of the invention, mammalian angiogenesis polypeptide is typically used, *e.g.*, mouse, preferably human.

A variety of angiogenesis assays are known to those of skill in the art. Various models have been employed to evaluate angiogenesis (*e.g.*, Croix *et al.*, *Science* 289:1197-1202, 2000 and Kahn *et al.*, *Amer. J. Pathol.* 156:1887-1900). Assessement of angiogenesis in the presence of a potential modulator of angiogenesis can be performed using cell-cultre-based angiogenesis assays, *e.g.*, endothelial cell tube formation assays, as well as other bioassays such as the chick CAM assay, the mouse corneal assay, and assays measuring the effect of administering potential modulators on implanted tumors. The chick CAM assay is described by O'Reilly, *et al.* Cell 79: 315-328, 1994. Briefly, 3 day old chicken embryos with intact yolks are separated from the egg and placed in a petri dish. After 3 days of incubation, a methylcellulose disc containing the protein to be tested is applied to the CAM of individual embryos. After about 48 hours of incubation, the embryos and CAMs are observed to determine whether endothelial growth has been inhibited. The mouse corneal assay involves implanting a growth factor-containing pellet, along with another pellet containing the suspected endothelial growth inhibitor, in the cornea of a mouse and observing the pattern of capillaries that are elaborated in the cornea. Angiogenesis can also be measured by determining the extent of neovascularization of a tumor. For example, carcinoma cells can be subcutaneously inoculated into athymic nude mice and tumor growth then monitored. The cancer cells are treated with an angiogenesis inhibitor, such as an antibody, or other compound that is exogenously administered, or can be transfected prior to inoculation with a polynucleotide inhibitor of angiogenesis. Immunoassays using endothelial cell-specific antibodies are typically used to stain for vascularization of tumor and the number of vessels in the tumor.

Assays to identify compounds with modulating activity can be performed *in vitro*. For example, an angiogenesis polypeptide is first contacted with a potential modulator and incubated for a suitable amount of time, *e.g.*, from 0.5 to 48 hours. In one embodiment, the angiogenesis polypeptide levels are determined *in vitro* by measuring the level of protein or mRNA. The level of protein is measured using immunoassays such as western blotting, ELISA and the like with an antibody that selectively binds to the angiogenesis polypeptide or a fragment thereof. For measurement of mRNA, amplification, e.g., using PCR, LCR, or hybridization assays, e.g., northern hybridization, RNAse protection, dot blotting, are preferred. The level of protein or mRNA is detected using directly or indirectly labeled

detection agents, *e.g.*, fluorescently or radioactively labeled nucleic acids, radioactively or enzymatically labeled antibodies, and the like, as described herein.

Alternatively, a reporter gene system can be devised using the angiogenesis protein promoter operably linked to a reporter gene such as luciferase, green fluorescent protein, CAT, or β-gal. The reporter construct is typically transfected into a cell. After treatment with a potential modulator, the amount of reporter gene transcription, translation, or activity is measured according to standard techniques known to those of skill in the art.

In a preferred embodiment, as outlined above, screens may be done on individual genes and gene products (proteins). That is, having identified a particular differentially expressed gene as important in a particular state, screening of modulators of the expression of the gene or the gene product itself can be done. The gene products of differentially expressed genes are sometimes referred to herein as "angiogenesis proteins". In preferred embodiments the angiogenesis protein comprises a sequence shown in Table 2. The angiogenesis protein may be a fragment, or alternatively, be the full length protein to a fragment shown herein.

Preferably, the angiogenesis protein is a fragment of approximately 14 to 24 amino acids long. More preferably the fragment is a soluble fragment. In one embodiment an angiogenesis protein is conjugated to an immunogenic agent or BSA.

In one embodiment, screening for modulators of expression of specific genes is performed. Typically, the expression of only one or a few genes are evaluated. In another embodiment, screens are designed to first find compounds that bind to differentially expressed proteins. These compounds are then evaluated for the ability to modulate differentially expressed activity. Moreover, once initial candidate compounds are identified, variants can be further screened to better evaluate strucutre activity relationships.

In a preferred embodiment, binding assays are done. In general, purified or isolated gene product is used; that is, the gene products of one or more differentially expressed nucleic acids are made. For example, antibodies are generated to the protein gene products, and standard immunoassays are run to determine the amount of protein present. Alternatively, cells comprising the angiogenesis proteins can be used in the assays.

Thus, in a preferred embodiment, the methods comprise combining an angiogenesis protein and a candidate compound, and determining the binding of the compound to the angiogenesis protein. Preferred embodiments utilize the human angiogenesis protein, although other mammalian proteins may also be used, for example for

the development of animal models of human disease. In some embodiments, as outlined herein, variant or derivative angiogenesis proteins may be used.

Generally, in a preferred embodiment of the methods herein, the angiogenesis protein or the candidate agent is non-diffusably bound to an insoluble support having isolated sample receiving areas (e.g. a microtiter plate, an array, etc.). The insoluble supports may be made of any composition to which the compositions can be bound, is readily separated from soluble material, and is otherwise compatible with the overall method of screening. The surface of such supports may be solid or porous and of any convenient shape. Examples of suitable insoluble supports include microtiter plates, arrays, membranes and beads. These are typically made of glass, plastic (e.g., polystyrene), polysaccharides, nylon or nitrocellulose, teflon™, etc. Microtiter plates and arrays are especially convenient because a large number of assays can be carried out simultaneously, using small amounts of reagents and samples. The particular manner of binding of the composition is not crucial so long as it is compatible with the reagents and overall methods of the invention, maintains the activity of the composition and is nondiffusable. Preferred methods of binding include the use of antibodies (which do not sterically block either the ligand binding site or activation sequence when the protein is bound to the support), direct binding to "sticky" or ionic supports, chemical crosslinking, the synthesis of the protein or agent on the surface, etc. Following binding of the protein or agent, excess unbound material is removed by washing. The sample receiving areas may then be blocked through incubation with bovine serum albumin (BSA), casein or other innocuous protein or other moiety.

In a preferred embodiment, the angiogenesis protein is bound to the support, and a test compound is added to the assay. Alternatively, the candidate agent is bound to the support and the angiogenesis protein is added. Novel binding agents include specific antibodies, non-natural binding agents identified in screens of chemical libraries, peptide analogs, etc. Of particular interest are screening assays for agents that have a low toxicity for human cells. A wide variety of assays may be used for this purpose, including labeled in vitro protein-protein binding assays, electrophoretic mobility shift assays, immunoassays for protein binding, functional assays (phosphorylation assays, etc.) and the like.

The determination of the binding of the test modulating compound to the angiogenesis protein may be done in a number of ways. In a preferred embodiment, the compound is labelled, and binding determined directly, *e.g.*, by attaching all or a portion of the angiogenesis protein to a solid support, adding a labelled candidate agent (*e.g.*, a

fluorescent label), washing off excess reagent, and determining whether the label is present on the solid support. Various blocking and washing steps may be utilized as appropriate.

By "labeled" herein is meant that the compound is either directly or indirectly labeled with a label which provides a detectable signal, *e.g.* radioisotope, fluorescers, enzyme, antibodies, particles such as magnetic particles, chemiluminescers, or specific binding molecules, etc. Specific binding molecules include pairs, such as biotin and streptavidin, digoxin and antidigoxin, etc. For the specific binding members, the complementary member would normally be labeled with a molecule which provides for detection, in accordance with known procedures, as outlined above. The label can directly or indirectly provide a detectable signal.

In some embodiments, only one of the components is labeled, *e.g.*, the proteins (or proteinaceous candidate compounds) can be labeled. Alternatively, more than one component can be labeled with different labels, *e.g.*, ^{125}I for the proteinsand a fluorophor for the compound. Proximity reagents, *e.g.*, quenching or energy transfer reagents are also useful.

In one embodiment, the binding of the test compound is determined by competitive binding assay. The competitor is a binding moiety known to bind to the target molecule (*i.e.* an angiogenesis protein), such as an antibody, peptide, binding partner, ligand, etc. Under certain circumstances, there may be competitive binding between the compound and the binding moiety, with the binding moiety displacing the compound. In one embodiment, the test compound is labeled. Either the compound, or the competitor, or both, is added first to the protein for a time sufficient to allow binding, if present. Incubations may be performed at a temperature which facilitates optimal activity, typically between 4 and 40°C. Incubation periods are typically optimized, *e.g.*, to facilitate rapid high throughput screening. Typically between 0.1 and 1 hour will be sufficient. Excess reagent is generally removed or washed away. The second component is then added, and the presence or absence of the labeled component is followed, to indicate binding.

In a preferred embodiment, the competitor is added first, followed by the test compound. Displacement of the competitor is an indication that the test compound is binding to the angiogenesis protein and thus is capable of binding to, and potentially modulating, the activity of the angiogenesis protein. In this embodiment, either component can be labeled. Thus, for example, if the competitor is labeled, the presence of label in the wash solution indicates displacement by the agent. Alternatively, if the test compound is labeled, the presence of the label on the support indicates displacement.

In an alternative embodiment, the test compound is added first, with incubation and washing, followed by the competitor. The absence of binding by the competitor may indicate that the test compound is bound to the angiogenesis protein with a higher affinity. Thus, if the test compound is labeled, the presence of the label on the support, coupled with a lack of competitor binding, may indicate that the test compound is capable of binding to the angiogenesis protein.

In a preferred embodiment, the methods comprise differential screening to identity agents that are capable of modulating the activitity of the angiogenesis proteins. In this embodiment, the methods comprise combining an angiogenesis protein and a competitor in a first sample. A second sample comprises a test compound, an angiogenesis protein, and a competitor. The binding of the competitor is determined for both samples, and a change, or difference in binding between the two samples indicates the presence of an agent capable of binding to the angiogenesis protein and potentially modulating its activity. That is, if the binding of the competitor is different in the second sample relative to the first sample, the agent is capable of binding to the angiogenesis protein.

Alternatively, differential screening is used to identify drug candidates that bind to the native angiogenesis protein, but cannot bind to modified angiogenesis proteins. The structure of the angiogenesis protein may be modeled, and used in rational drug design to synthesize agents that interact with that site. Drug candidates that affect the activity of an angiogenesis protein are also identified by screening drugs for the ability to either enhance or reduce the activity of the protein.

Positive controls and negative controls may be used in the assays. Preferably control and test samples are performed in at least triplicate to obtain statistically significant results. Incubation of all samples is for a time sufficient for the binding of the agent to the protein. Following incubation, samples are washed free of non-specifically bound material and the amount of bound, generally labeled agent determined. For example, where a radiolabel is employed, the samples may be counted in a scintillation counter to determine the amount of bound compound.

A variety of other reagents may be included in the screening assays. These include reagents like salts, neutral proteins, *e.g.* albumin, detergents, *etc.* which may be used to facilitate optimal protein-protein binding and/or reduce non-specific or background interactions. Also reagents that otherwise improve the efficiency of the assay, such as protease inhibitors, nuclease inhibitors, anti-microbial agents, etc., may be used. The mixture of components may be added in an order that provides for the requisite binding.

In a preferred embodiment, the invention provides methods for screening for a compound capable of modulating the activity of an angiogenesis protein. The methods comprise adding a test compound, as defined above, to a cell comprising angiogenesis proteins. Preferred cell types include almost any cell. The cells contain a recombinant nucleic acid that encodes an angiogenesis protein. In a preferred embodiment, a library of candidate agents are tested on a plurality of cells.

In one aspect, the assays are evaluated in the presence or absence or previous or subsequent exposure of physiological signals, for example hormones, antibodies, peptides, antigens, cytokines, growth factors, action potentials, pharmacological agents including chemotherapeutics, radiation, carcinogenics, or other cells (i.e. cell-cell contacts). In another example, the determinations are determined at different stages of the cell cycle process.

In this way, compounds that modulate angiogenesis agents are identified. Compounds with pharmacological activity are able to enhance or interfere with the activity of the angiogenesis protein. Once identified, similar structures are evaluated to identify critical structural feature of the compound.

In one embodiment, a method of inhibiting angiogenic cell division is provided. The method comprises administration of an angiogenesis inhibitor. In another embodiment, a method of inhibiting angiogenesis is provided. The method comprises administration of an angiogenesis inhibitor. In a further embodiment, methods of treating cells or individuals with angiogenesis are provided. The method comprises administration of an angiogenesis inhibitor.

In one embodiment, an angiogenesis inhibitor is an antibody as discussed above. In another embodiment, the angiogenesis inhibitor is an antisense molecule.

Polynucleotide modulators of angiogenesis

Antisense Polynucleotides

In certain embodiments, the activity of an angiogenesis-associated protein is downregulated, or entirely inhibited, by the use of antisense polynucleotide, *i.e.*, a nucleic acid complementary to, and which can preferably hybridize specifically to, a coding mRNA nucleic acid sequence, *e.g.*, an angiogenesis protein mRNA, or a subsequence thereof. Binding of the antisense polynucleotide to the mRNA reduces the translation and/or stability of the mRNA.

In the context of this invention, antisense polynucleotides can comprise naturally-occurring nucleotides, or synthetic species formed from naturally-occurring

subunits or their close homologs. Antisense polynucleotides may also have altered sugar moieties or inter-sugar linkages. Exemplary among these are the phosphorothioate and other sulfur containing species which are known for use in the art. Analogs are comprehended by this invention so long as they function effectively to hybridize with the angiogenesis protein mRNA. See, *e.g.*, Isis Pharmaceuticals, Carlsbad, CA; Sequitor, Inc., Natick, MA.

Such antisense polynucleotides can readily be synthesized using recombinant means, or can be synthesized *in vitro*. Equipment for such synthesis is sold by several vendors, including Applied Biosystems. The preparation of other oligonucleotides such as phosphorothioates and alkylated derivatives is also well known to those of skill in the art.

Antisense molecules as used herein include antisense or sense oligonucleotides. Sense oligonucleotides can, *e.g.*, be employed to block trancription by binding to the anti-sense strand. The antisense and sense oligonucleotide comprise a single-stranded nucleic acid sequence (either RNA or DNA) capable of binding to target mRNA (sense) or DNA (antisense) sequences for angiogenesis molecules. A preferred antisense molecule is for an angiogenesis sequences in Table 1, or for a ligand or activator thereof. Antisense or sense oligonucleotides, according to the present invention, comprise a fragment generally at least about 14 nucleotides, preferably from about 14 to 30 nucleotides. The ability to derive an antisense or a sense oligonucleotide, based upon a cDNA sequence encoding a given protein is described in, for example, Stein and Cohen (Cancer Res. 48:2659, 1988) and van der Krol et al. (BioTechniques 6:958, 1988).

Ribozymes

In addition to antisense polynucleotides, ribozymes can be used to target and inhibit transcription of angiogenesis-associated nucleotide sequences. A ribozyme is an RNA molecule that catalytically cleaves other RNA molecules. Different kinds of ribozymes have been described, including group I ribozymes, hammerhead ribozymes, hairpin ribozymes, RNase P, and axhead ribozymes (*see, e.g.,* Castanotto *et al.* (1994) *Adv. in Pharmacology* 25: 289-317 for a general review of the properties of different ribozymes).

The general features of hairpin ribozymes are described, *e.g.*, in Hampel *et al.* (1990) *Nucl. Acids Res.* 18: 299-304; Hampel *et al.* (1990) European Patent Publication No. 0 360 257; U.S. Patent No. 5,254,678. Methods of preparing are well known to those of skill in the art (*see, e.g.,* Wong-Staal *et al.*, WO 94/26877; Ojwang *et al.* (1993) *Proc. Natl. Acad. Sci.* USA 90: 6340-6344; Yamada *et al.* (1994) *Human Gene Therapy* 1: 39-45; Leavitt *et al.*

(1995) *Proc. Natl. Acad. Sci. USA* 92: 699-703; Leavitt *et al.* (1994) *Human Gene Therapy* 5: 1151-120; and Yamada *et al.* (1994) *Virology* 205: 121-126).

Polynucleotide modulators of angiogenesis may be introduced into a cell containing the target nucleotide sequence by formation of a conjugate with a ligand binding molecule, as described in WO 91/04753. Suitable ligand binding molecules include, but are not limited to, cell surface receptors, growth factors, other cytokines, or other ligands that bind to cell surface receptors. Preferably, conjugation of the ligand binding molecule does not substantially interfere with the ability of the ligand binding molecule to bind to its corresponding molecule or receptor, or block entry of the sense or antisense oligonucleotide or its conjugated version into the cell. Alternatively, a polynucleotide modulator of angiogenesis may be introduced into a cell containing the target nucleic acid sequence, *e.g.*, by formation of an polynucleotide-lipid complex, as described in WO 90/10448. It is understood that the use of antisense molecules or knock out and knock in models may also be used in screening assays as discussed above, in addition to methods of treatment.

Thus, in one embodiment, methods of modulating angiogenesis in cells or organisms are provided. In one embodiment, the methods comprise administering to a cell an anti-angiogenesis antibody that reduces or eliminates the biological activity of an endogeneous angiogenesis protein. Alternatively, the methods comprise administering to a cell or organism a recombinant nucleic acid encoding an angiogenesis protein. This may be accomplished in any number of ways. In a preferred embodiment, for example when the angiogenesis sequence is down-regulated in angiogenesis, such state may be reversed by increasing the amount of angiogenesis gene product in the cell. This can be accomplished, *e.g.*, by overexpressing the endogeneous angiogenesis gene or administering a gene encoding the angiogenesis sequence, using known gene-therapy techniques, for example. In a preferred embodiment, the gene therapy techniques include the incorporation of the exogenous gene using enhanced homologous recombination (EHR), for example as described in PCT/US93/03868, hereby incorporated by reference in its entireity. Alternatively, for example when the angiogenesis sequence is up-regulated in angiogenesis, the activity of the endogeneous angiogenesis gene is decreased, for example by the administration of a angiogenesis antisense nucleic acid.

In one embodiment, the angiogenesis proteins of the present invention may be used to generate polyclonal and monoclonal antibodies to angiogenesis proteins. Similarly, the angiogenesis proteins can be coupled, using standard technology, to affinity chromatography columns. These columns may then be used to purify angiogenesis

antibodies useful for production, diagnostic, or therapeutic purposes. In a preferred embodiment, the antibodies are generated to epitopes unique to a angiogenesis protein; that is, the antibodies show little or no cross-reactivity to other proteins. The angiogenesis antibodies may be coupled to standard affinity chromatography columns and used to purify angiogenesis proteins. The antibodies may also be used as blocking polypeptides, as outlined above, since they will specifically bind to the angiogenesis protein.

Methods of identifying variant angiogenesis-associated sequences

Without being bound by theory, expression of various angiogenesis sequences is correlated with angiogenesis. Accordingly, disorders based on mutant or variant angiogenesis genes may be determined. In one embodiment, the invention provides methods for identifying cells containing variant angiogenesis genes, *e.g.*, determining all or part of the sequence of at least one endogeneous angiogenesis genes in a cell. This may be accomplished using any number of sequencing techniques. In a preferred embodiment, the invention provides methods of identifying the angiogenesis genotype of an individual, *e.g.*, determining all or part of the sequence of at least one angiogenesis gene of the individual. This is generally done in at least one tissue of the individual, and may include the evaluation of a number of tissues or different samples of the same tissue. The method may include comparing the sequence of the sequenced angiogenesis gene to a known angiogenesis gene, *i.e.*, a wild-type gene.

The sequence of all or part of the angiogenesis gene can then be compared to the sequence of a known angiogenesis gene to determine if any differences exist. This can be done using any number of known homology programs, such as Bestfit, etc. In a preferred embodiment, the presence of a a difference in the sequence between the angiogenesis gene of the patient and the known angiogenesis gene correlates with a disease state or a propensity for a disease state, as outlined herein.

In a preferred embodiment, the angiogenesis genes are used as probes to determine the number of copies of the angiogenesis gene in the genome.

In another preferred embodiment, the angiogenesis genes are used as probes to determine the chromosomal localization of the angiogenesis genes. Information such as chromosomal localization finds use in providing a diagnosis or prognosis in particular when chromosomal abnormalities such as translocations, and the like are identified in the angiogenesis gene locus.

Administration of pharmaceutical and vaccine compositions

In one embodiment, a therapeutically effective dose of an angiogenesis protein or modulator thereof, is administered to a patient. By "therapeutically effective dose" herein is meant a dose that produces effects for which it is administered. The exact dose will depend on the purpose of the treatment, and will be ascertainable by one skilled in the art using known techniques (*e.g.*, Ansel *et al.*, Pharmaceuitcal Dosage Forms and Drug Delivery, Lippincott, Williams & Wilkins Publishers, ISBN:0683305727; Lieberman (1992) Pharmaceutical Dosage Forms (vols. 1-3), Dekker, ISBN 0824770846, 082476918X, 0824712692, 0824716981; Lloyd (1999) The Art, Science and Technology of Pharmaceutical Compounding, Amer. Pharmacutical Assn, ISBN 0917330889; and Pickar (1999) Dosage Calculations, Delmar Pub, ISBN 0766805042). As is known in the art, adjustments for angiogenesis degradation, systemic versus localized delivery, and rate of new protease synthesis, as well as the age, body weight, general health, sex, diet, time of administration, drug interaction and the severity of the condition may be necessary, and will be ascertainable with routine experimentation by those skilled in the art.

A "patient" for the purposes of the present invention includes both humans and other animals, particularly mammals. Thus the methods are applicable to both human therapy and veterinary applications. In the preferred embodiment the patient is a mammal, preferably a primate, and in the most preferred embodiment the patient is human.

The administration of the angiogenesis proteins and modulators thereof of the present invention can be done in a variety of ways as discussed above, including, but not limited to, orally, subcutaneously, intravenously, intranasally, transdermally, intraperitoneally, intramuscularly, intrapulmonary, vaginally, rectally, or intraocularly. In some instances, for example, in the treatment of wounds and inflammation, the angiogenesis proteins and modulators may be directly applied as a solution or spray.

The pharmaceutical compositions of the present invention comprise an angiogenesis protein in a form suitable for administration to a patient. In the preferred embodiment, the pharmaceutical compositions are in a water soluble form, such as being present as pharmaceutically acceptable salts, which is meant to include both acid and base addition salts. "Pharmaceutically acceptable acid addition salt" refers to those salts that retain the biological effectiveness of the free bases and that are not biologically or otherwise undesirable, formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid and the like, and organic acids such as acetic acid, propionic acid, glycolic acid, pyruvic acid, oxalic acid, maleic acid, malonic acid, succinic

acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid and the like. "Pharmaceutically acceptable base addition salts" include those derived from inorganic bases such as sodium, potassium, lithium, ammonium, calcium, magnesium, iron, zinc, copper, manganese, aluminum salts and the like. Particularly preferred are the ammonium, potassium, sodium, calcium, and magnesium salts. Salts derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins, such as isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, and ethanolamine.

The pharmaceutical compositions may also include one or more of the following: carrier proteins such as serum albumin; buffers; fillers such as microcrystalline cellulose, lactose, corn and other starches; binding agents; sweeteners and other flavoring agents; coloring agents; and polyethylene glycol.

The pharmaceutical compositions can be administered in a variety of unit dosage forms depending upon the method of administration. For example, unit dosage forms suitable for oral administration include, but are not limited to, powder, tablets, pills, capsules and lozenges. It is recognized that angiogenesis protein modulators (*e.g.*, antibodies, antisense constructs, ribozymes, small organic molecules, *etc.*) when administered orally, should be protected from digestion. This is typically accomplished either by complexing the molecule(s) with a composition to render it resistant to acidic and enzymatic hydrolysis, or by packaging the molecule(s) in an appropriately resistant carrier, such as a liposome or a protection barrier. Means of protecting agents from digestion are well known in the art.

The compositions for administration will commonly comprise an angiogenesis protein modulator dissolved in a pharmaceutically acceptable carrier, preferably an aqueous carrier. A variety of aqueous carriers can be used, *e.g.*, buffered saline and the like. These solutions are sterile and generally free of undesirable matter. These compositions may be sterilized by conventional, well known sterilization techniques. The compositions may contain pharmaceutically acceptable auxiliary substances as required to approximate physiological conditions such as pH adjusting and buffering agents, toxicity adjusting agents and the like, for example, sodium acetate, sodium chloride, potassium chloride, calcium chloride, sodium lactate and the like. The concentration of active agent in these formulations can vary widely, and will be selected primarily based on fluid volumes, viscosities, body weight and the like in accordance with the particular mode of administration selected and the

patient's needs (*e.g.*, *Remington's Pharmaceutical Science*, 15th ed., Mack Publishing Company, Easton, Pennsylvania (1980) and Goodman and Gillman, *The Pharmacologial Basis of Therapeutics*,(Hardman, J.G, Limbird, L.E, Molinoff, P.B., Ruddon, R.W, and Gilman, A.G.,eds) TheMcGraw-Hill Companies, Inc.,1996).

Thus, a typical pharmaceutical composition for intravenous administration would be about 0.1 to 10 mg per patient per day. Dosages from 0.1 up to about 100 mg per patient per day may be used, particularly when the drug is administered to a secluded site and not into the blood stream, such as into a body cavity or into a lumen of an organ. Substantially higher dosages are possible in topical administration. Actual methods for preparing parenterally administrable compositions will be known or apparent to those skilled in the art, *e.g.*, *Remington's Pharmaceutical Science* and Goodman and Gillman, *The Pharmacologial Basis of Therapeutics*, *supra*.

The compositions containing modulators of angiogenesis proteins can be administered for therapeutic or prophylactic treatments. In therapeutic applications, compositions are administered to a patient suffering from a disease (*e.g.*, a cancer) in an amount sufficient to cure or at least partially arrest the disease and its complications. An amount adequate to accomplish this is defined as a "therapeutically effective dose." Amounts effective for this use will depend upon the severity of the disease and the general state of the patient's health. Single or multiple administrations of the compositions may be administered depending on the dosage and frequency as required and tolerated by the patient. In any event, the composition should provide a sufficient quantity of the agents of this invention to effectively treat the patient. An amount of modulator that is capable of preventing or slowing the development of cancer in a mammal is referred to as a "prophylactically effective dose." The particular dose required for a prophylactic treatment will depend upon the medical condition and history of the mammal, the particular cancer being prevented, as well as other factors such as age, weight, gender, administration route, efficiency, *etc.* Such prophylactic treatments may be used, *e.g.*, in a mammal who has previously had cancer to prevent a recurrence of the cancer, or in a mammal who is suspected of having a significant likelihood of developing cancer.

It will be appreciated that the present angiogenesis protein-modulating compounds can be administered alone or in combination with additional angiogenesis modulating compounds or with other therapeutic agent, *e.g.*, other anti-cancer agents or treatments.

In numerous embodiments, one or more nucleic acids, *e.g.*, polynucleotides comprising nucleic acid sequences set forth in Table 1, such as antisense polynucleotides or ribozymes, will be introduced into cells, *in vitro* or *in vivo*. The present invention provides methods, reagents, vectors, and cells useful for expression of angiogenesis-associated polypeptides and nucleic acids using *in vitro* (cell-free), *ex vivo* or *in vivo* (cell or organism-based) recombinant expression systems.

The particular procedure used to introduce the nucleic acids into a host cell for expression of a protein or nucleic acid is application specific. Many procedures for introducing foreign nucleotide sequences into host cells may be used. These include the use of calcium phosphate transfection, spheroplasts, electroporation, liposomes, microinjection, plasma vectors, viral vectors and any of the other well known methods for introducing cloned genomic DNA, cDNA, synthetic DNA or other foreign genetic material into a host cell (*see, e.g.*, Berger and Kimmel, *Guide to Molecular Cloning Techniques, Methods in Enzymology* volume 152 Academic Press, Inc., San Diego, CA (Berger), F.M. Ausubel *et al.*, eds., Current Protocols, a joint venture between Greene Publishing Associates, Inc. and John Wiley & Sons, Inc., (supplemented through 1999), and Sambrook *et al.*, *Molecular Cloning - A Laboratory Manual* (2nd Ed.), Vol. 1-3, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, 1989.

In a preferred embodiment, angiogenesis proteins and modulators are administered as therapeutic agents, and can be formulated as outlined above. Similarly, angiogenesis genes (including both the full-length sequence, partial sequences, or regulatory sequences of the angiogenesis coding regions) can be administered in a gene therapy application. These angiogenesis genes can include antisense applications, either as gene therapy (i.e. for incorporation into the genome) or as antisense compositions, as will be appreciated by those in the art.

Angiogenesis polypeptides and polynucleotides can also be administered as vaccine compositions to stimulate HTL, CTL and antibody responses.. Such vaccine compositions can include, for example, lipidated peptides (*e.g.*,Vitiello, A. *et al.*, *J. Clin. Invest.* 95:341, 1995), peptide compositions encapsulated in poly(DL-lactide-co-glycolide) ("PLG") microspheres (*see, e.g.*, Eldridge, *et al.*, *Molec. Immunol.* 28:287-294, 1991: Alonso *et al.*, *Vaccine* 12:299-306, 1994; Jones *et al.*, *Vaccine* 13:675-681, 1995), peptide compositions contained in immune stimulating complexes (ISCOMS) (*see, e.g.*, Takahashi *et al.*, *Nature* 344:873-875, 1990; Hu *et al.*, *Clin Exp Immunol.* 113:235-243, 1998), multiple antigen peptide systems (MAPs) (*see e.g.*, Tam, J. P., *Proc. Natl. Acad. Sci. U.S.A.* 85:5409-

5413, 1988; Tam, J.P., *J. Immunol. Methods* 196:17-32, 1996), peptides formulated as multivalent peptides; peptides for use in ballistic delivery systems, typically crystallized peptides, viral delivery vectors (Perkus, M. E. *et al.*, In: *Concepts in vaccine development*, Kaufmann, S. H. E., ed., p. 379, 1996; Chakrabarti, S. *et al.*, *Nature* 320:535, 1986; Hu, S. L. *et al.*, *Nature* 320:537, 1986; Kieny, M.-P. *et al.*, *AIDS Bio/Technology* 4:790, 1986; Top, F. H. *et al.*, *J. Infect. Dis.* 124:148, 1971; Chanda, P. K. *et al.*, *Virology* 175:535, 1990), particles of viral or synthetic origin (*e.g.*, Kofler, N. *et al.*, *J. Immunol. Methods.* 192:25, 1996; Eldridge, J. H. *et al.*, *Sem. Hematol.* 30:16, 1993; Falo, L. D., Jr. *et al.*, *Nature Med.* 7:649, 1995), adjuvants (Warren, H. S., Vogel, F. R., and Chedid, L. A. *Annu. Rev. Immunol.* 4:369, 1986; Gupta, R. K. *et al.*, *Vaccine* 11:293, 1993), liposomes (Reddy, R. *et al.*, *J. Immunol.* 148:1585, 1992; Rock, K. L., *Immunol. Today* 17:131, 1996), or, naked or particle absorbed cDNA (Ulmer, J. B. *et al.*, *Science* 259:1745, 1993; Robinson, H. L., Hunt, L. A., and Webster, R. G., *Vaccine* 11:957, 1993; Shiver, J. W. *et al.*, In: *Concepts in vaccine development*, Kaufmann, S. H. E., ed., p. 423, 1996; Cease, K. B., and Berzofsky, J. A., *Annu. Rev. Immunol.* 12:923, 1994 and Eldridge, J. H. *et al.*, *Sem. Hematol.* 30:16, 1993). Toxin-targeted delivery technologies, also known as receptor mediated targeting, such as those of Avant Immunotherapeutics, Inc. (Needham, Massachusetts) may also be used.

Vaccine compositions often include adjuvants. Many adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bortadella pertussis* or *Mycobacterium tuberculosis* derived proteins. Certain adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF, interleukin-2, -7, -12, and other like growth factors, may also be used as adjuvants.

Vaccines can be administered as nucleic acid compositions wherein DNA or RNA encoding one or more of the polypeptides, or a fragment thereof, is administered to a patient. This approach is described, for instance, in Wolff *et. al.*, *Science* 247:1465 (1990) as well as U.S. Patent Nos. 5,580,859; 5,589,466; 5,804,566; 5,739,118; 5,736,524; 5,679,647; WO 98/04720; and in more detail below. Examples of DNA-based delivery technologies

include "naked DNA", facilitated (bupivicaine, polymers, peptide-mediated) delivery, cationic lipid complexes, and particle-mediated ("gene gun") or pressure-mediated delivery (*see, e.g.*, U.S. Patent No. 5,922,687).

For therapeutic or prophylactic immunization purposes, the peptides of the invention can be expressed by viral or bacterial vectors. Examples of expression vectors include attenuated viral hosts, such as vaccinia or fowlpox. This approach involves the use of vaccinia virus, for example, as a vector to express nucleotide sequences that encode angiogenic polypeptides or polypeptide fragments. Upon introduction into a host, the recombinant vaccinia virus expresses the immunogenic peptide, and thereby elicits an immune response. Vaccinia vectors and methods useful in immunization protocols are described in, *e.g.*, U.S. Patent No. 4,722,848. Another vector is BCG (Bacille Calmette Guerin). BCG vectors are described in Stover *et al.*, *Nature* 351:456-460 (1991). A wide variety of other vectors useful for therapeutic administration or immunization *e.g.* adeno and adeno-associated virus vectors, retroviral vectors, *Salmonella typhi* vectors, detoxified anthrax toxin vectors, and the like, will be apparent to those skilled in the art from the description herein (see, *e.g.*, Shata *et al.* (2000) Mol Med Today, 6: 66-71; Shedlock *et al.*, *J Leukoc Biol* 68,:793-806, 2000; Hipp *et al.*, *In Vivo* 14:571-85, 2000).

Methods for the use of genes as DNA vaccines are well known, and include placing an angiogenesis gene or portion of an angiogenesis gene under the control of a regulatable promoter or a tissue-specific promoter for expression in an angiogenesis patient. The angiogenesis gene used for DNA vaccines can encode full-length angiogenesis proteins, but more preferably encodes portions of the angiogenesis proteins including peptides derived from the angiogenesis protein. In one embodiment, a patient is immunized with a DNA vaccine comprising a plurality of nucleotide sequences derived from an angiogenesis gene. For example, angiogenesis-associated genes or sequence encoding subfragments of an angiogenesis protein are introduced into expression vectors and tested for their immunogenicity in the context of Class I MHC and an ability to generate cytotoxic T cell responses. This procedure provides for production of cytotoxic T cell responses against cells which present antigen, including intracellular epitopes.

In a preferred embodiment, the DNA vaccines include a gene encoding an adjuvant molecule with the DNA vaccine. Such adjuvant molecules include cytokines that increase the immunogenic response to the angiogenesis polypeptide encoded by the DNA vaccine. Additional or alternative adjuvants are available.

In another preferred embodiment angiogenesis genes find use in generating animal models of angiogenesis. When the angiogenesis gene identified is repressed or diminished in angiogenesic tissue, gene therapy technology, *e.g.*, wherein antisense RNA directed to the angiogenesis gene will also diminish or repress expression of the gene. Animal models of angiogenesis find use in screening for modulators of an angiogenesis-associated sequence or modulators of angiogenesis. Similarly, transgenic animal technology including gene knockout technology, for example as a result of homologous recombination with an appropriate gene targeting vector, will result in the absence or increased expression of the angiogenesis protein. When desired, tissue-specific expression or knockout of the angiogenesis protein may be necessary.

It is also possible that the angiogenesis protein is overexpressed in angiogenesis. As such, transgenic animals can be generated that overexpress the angiogenesis protein. Depending on the desired expression level, promoters of various strengths can be employed to express the transgene. Also, the number of copies of the integrated transgene can be determined and compared for a determination of the expression level of the transgene. Animals generated by such methods find use as animal models of angiogenesis and are additionally useful in screening for modulators to treat angiogenesis.

Kits for Use in Diagnostic and/or Prognostic Applications

For use in diagnostic, research, and therapeutic applications suggested above, kits are also provided by the invention. In the diagnostic and research applications such kits may include any or all of the following: assay reagents, buffers, angiogenesis-specific nucleic acids or antibodies, hybridization probes and/or primers, antisense polynucleotides, ribozymes, dominant negative angiogenesis polypeptides or polynucleotides, small molecules inhibitors of angiogenesis-associated sequences *etc.* A therapeutic product may include sterile saline or another pharmaceutically acceptable emulsion and suspension base.

In addition, the kits may include instructional materials containing directions (*i.e.*, protocols) for the practice of the methods of this invention. While the instructional materials typically comprise written or printed materials they are not limited to such. Any medium capable of storing such instructions and communicating them to an end user is contemplated by this invention. Such media include, but are not limited to electronic storage media (*e.g.*, magnetic discs, tapes, cartridges, chips), optical media (*e.g.*, CD ROM), and the like. Such media may include addresses to internet sites that provide such instructional materials.

The present invention also provides for kits for screening for modulators of angiogenesis-associated sequences. Such kits can be prepared from readily available materials and reagents. For example, such kits can comprise one or more of the following materials: an angiogenesis-associated polypeptide or polynucleotide, reaction tubes, and instructions for testing angiogenic-associated activity. Optionally, the kit contains biologically active angiogenesis protein. A wide variety of kits and components can be prepared according to the present invention, depending upon the intended user of the kit and the particular needs of the user. Diagnosis would typically involve evaluation of a plurality of genes or products. The genes will be selected based on correlations with important parameters in disease which may be identified in historical or outcome data.

It is understood that the examples described above in no way serve to limit the true scope of this invention, but rather are presented for illustrative purposes. All publications, sequences of accession numbers, and patent applications cited in this specification are herein incorporated by reference as if each individual publication or patent application were specifically and individually indicated to be incorporated by reference.

EXAMPLES

Example 1: Tissue Preparation, Labeling Chips, and Fingerprints

Purify total RNA from tissue using TRIzol Reagent

Homogenize tissue samples in 1ml of TRIzol per 50mg of tissue using a Polytron 3100 homogenizer. The generator/probe used depends upon the tissue size. A generator that is too large for the amount of tissue to be homogenized will cause a loss of sample and lower RNA yield. TRIzol is added directly to frozen tissue, which is then homogenize. Following homogenization, insoluble material is removed by centrifugation at 7500 x g for 15 min in a Sorvall superspeed or 12,000 x g for 10 min. in an Eppendorf centrifuge at 4°C. The clear homogenate is transferred to a new tube for use. The samples may be frozen now at -60° to -70°C (and kept for at least one month). The homogenate is mixed with 0.2ml of chloroform per 1ml of TRIzol reagent used in the original homogenization and incubated at room temp. for 2-3 minutes. The aqueous phase is then separated by centrifugation and transferred to a fresh tube and the RNA precipitated using isopropyl alcohol. The pellet is isolated by centrifugation, washed, air-dried, resuspended in an appropriate volume of DEPC H_20, and the absorbance measured.

Purification of poly A+ mRNA from total RNA is performed as follows. Heat an oligotex suspension to 37°C and mixing immediately before adding to RNA. The Elution Buffer is heated at 70°C. Warm up 2 x Binding Buffer at 65°C if there is precipitate in the buffer. Mix total RNA with DEPC-treated water, 2 x Binding Buffer, and Oligotex according to Table 2 on page 16 of the Oligotex Handbook. Incubate for 3 minutes at 65°C. Incubate for 10 minutes at room temperature. Centrifuge for 2 minutes at 14,000 to 18,000 g. Remove supernatant without disturbing Oligotex pellet. A little bit of solution can be left behind to reduce the loss of Oligotex. Gently resuspend in Wash Buffer OW2 and pipet onto spin column. Centrifuge the spin column at full speed for 1 minute. Transfer spin column to a new collection tube and gently resuspend in Wash Buffer OW2 and centrifuge as describe herein. Transfer spin column to a new tube and elute with 20 to 100 ul of preheated (70oC) Elution Buffer. Gently resuspend Oligotex resin by pipetting up and down. Centrifuge as above. Repeat elution with fresh elution buffer or use first eluate to keep the elution volume low. Read absorbance, using diluted Elution Buffer as the blank. Before proceeding with cDNA synthesis, precipitate the mRNA as follows: add 0.4 vol. of 7.5 M NH4OAc + 2.5 vol. of cold 100% ethanol. Precipitate at -20oC 1 hour to overnight (or 20-30 min. at -70oC). Centrifuge at 14,000-16,000 x g for 30 minutes at 4oC. Wash pellet with 0.5ml of 80%ethanol (-20oC) then centrifuge at 14,000-16,000 x g for 5 minutes at room temperature. Repeat 80% ethanol wash. Air dry the ethanol from the pellet in the hood.. Suspend pellet in DEPC H_20 at 1ug/ul concentration.

To further Clean up total RNA using Qiagen's RNeasy kit, add no more than 100ug to an RNeasy column. Adjust sample to a volume of 100ul with RNase-free water. Add 350ul Buffer RLT then 250ul ethanol (100%) to the sample. Mix by pipetting (do not centrifuge) then apply sample to an RNeasy mini spin column. Centrifuge for 15 sec at >10,000rpm. Transfer column to a new 2-ml collection tube. Add 500ul Buffer RPE and centrifuge for 15 sec at >10,000rpm. Discard flowthrough. Add 500ul Buffer RPE and centrifuge for 15 sec at >10,000rpm. Discard flowthrough then centrifuge for 2 min at maximum speed to dry column membrane. Transfer column to a new 1.5-ml collection tube and apply 30-50ul of RNase-free water directly onto column membrane. Centrifuge 1 min at >10,000rpm. Repeat elution. and read absorbance.

cDNA synthesis using Gibco's "SuperScript Choice System for cDNA Synthesis" kit

First Strand cDNA synthesis is performed as follows. Use 5ug of total RNA or 1ug of polyA+ mRNA as starting material. For total RNA, use 2ul of SuperScript RT. For

polyA+ mRNA, use 1ul of SuperScript RT. Final volume of first strand synthesis mix is 20ul. RNA must be in a volume no greater than 10ul. Incubate RNA with 1ul of 100pmol T7-T24 oligo for 10 min at 70C. On ice, add 7 ul of: 4ul 5X 1st Strand Buffer, 2ul of 0.1M DTT, and 1 ul of 10mM dNTP mix. Incubate at 37C for 2 min then add SuperScript RT. Incubate at 37C for 1 hour.

For the second strand synthesis, place 1st strand reactions on ice and add: 91ul DEPC H_20; 30ul 5X 2nd Strand Buffer; 3ul 10mM dNTP mix; 1ul 10U/ul E.coli DNA Ligase; 4ul 10U/ul E.coli DNA Polymerase; and 1ul 2U/ul RNase H. Mix and incubate 2 hours at 16C. Add 2ul T4 DNA Polymerase. Incubate 5 min at 16C. Add 10ul of 0.5M EDTA. A further clean-up of DNA is performed using phenol:chloroform:isoamyl Alcohol (25:24:1) purification.

In vitro Transcription (IVT) and labeling with biotin is performed as follows: Pipet 1.5ul of cDNA into a thin-wall PCR tube. Make NTP labeling mix by combining 2ul T7 10xATP (75mM) (Ambion); 2ul T7 10xGTP (75mM) (Ambion); 1.5ul T7 10xCTP (75mM) (Ambion); 1.5ul T7 10xUTP (75mM) (Ambion); 3.75ul 10mM Bio-11-UTP (Boehringer-Mannheim/Roche or Enzo); 3.75ul 10mM Bio-16-CTP (Enzo); 2ul 10x T7 transcription buffer (Ambion); and 2ul 10x T7 enzyme mix (Ambion). The final volume is 20ul. Incubate 6 hours at 37°C in a PCR machine. The RNA can be furthered cleaned.

Fragmentation is performed as follows. 15 ug of labeled RNA is usually fragmented. Try to minimize the fragmentation reaction volume; a 10 ul volume is recommended but 20 ul is all right. Do not go higher than 20 ul because the magnesium in the fragmentation buffer contributes to precipitation in the hybridization buffer. Fragment RNA by incubation at 94 C for 35 minutes in 1 x Fragmentation buffer (5 x Fragmentation buffer is 200 mM Tris-acetate, pH 8.1; 500 mM KOAc; 150 mM MgOAc). The labeled RNA transcript can be analyzed before and after fragmentation. Samples can be heated to 65°C for 15 minutes and electrophoresed on 1% agarose/TBE gels to get an approximate idea of the transcript size range

For hybridization, 200 ul (10ug cRNA) of a hybridization mix is put on the chip. If multiple hybridizations are to be done (such as cycling through a 5 chip set), then it is recommended that an initial hybridization mix of 300 ul or more be made. The hybridization mix is: fragment labeled RNA (50ng/ul final conc.); 50 pM 948-b control oligo; 1.5 pM BioB; 5 pM BioC; 25 pM BioD; 100 pM CRE; 0.1mg/ml herring sperm DNA; 0.5mg/ml acetylated BSA; and 300 ul with 1xMES hyb buffer.

Labeling is performed as follows: The hybridization reaction includes non-biotinylated IVT (purified by RNeasy columns); IVT antisense RNA 4 μg:μl; random Hexamers (1 μg/μl) 4 μl and water to 14 ul. The reaciton is incubated at 70°C, 10 min. Reverse transcriptionis performed in the following reaction: 5X First Strand (BRL) buffer, 6 μl; 0.1 M DTT, 3 μl; 50X dNTP mix, 0.6 μl; H_2O, 2.4 μl; Cy3 or Cy5 dUTP (1mM), 3 μl; SS RT II (BRL), 1 μl in a final volume of 16 μl. Add to hybridization reaction. Incubate 30 min., 42°C. Add 1 μl SSII and incubate another hour. Put on ice. 50X dNTP mix (25mM of cold dATP, dCTP, and dGTP, 10mM of dTTP: 25 μl each of 100mM dATP, dCTP, and dGTP; 10 μl of 100mM dTTP to 15 μl H2O. dNTPs from Pharmacia)

RNA degradation is performed as follows. Add 86 μl H2O, 1.5 μl 1M NaOH/ 2mM EDTA and incubate at 65°C, 10 min.. For U-Con 30, 500 μl TE/sample spin at 7000g for 10 min, save flow through for purification. For Qiagen purification, suspend u-con recovered material in 500μl buffer PB and proceed using Qiagen protocol. For DNAse digestion, add 1 ul of 1/100 dil of DNAse/30ul Rx and incubate at 37°C for 15 min. Incubate at 5 min 95°C to denature the DNAse/

For sample preparation, add Cot-1 DNA, 10 μl; 50X dNTPs, 1 μl; 20X SSC, 2.3 μl; Na pyro phosphate, 7.5 μl; 10mg/ml Herring sperm DNA; 1ul of 1/10 dilution to 21.8 final vol. Dry in speed vac. Resuspend in 15 μl H20. Add 0.38 μl 10% SDS. Heat 95°C, 2 min and slow cool at room temp. for 20 min. Put on slide and hybridize overnight at 64°C. Washing after the hybridization: 3X SSC/0.03% SDS: 2 min., 37.5 mls 20X SSC+0.75mls 10% SDS in 250mls H2O; 1X SSC: 5 min., 12.5 mls 20X SSC in 250mls H2O; 0.2X SSC: 5 min., 2.5 mls 20X SSC in 250mls H2O. Dry slides and scan at appropiate PMT's and channels.

Example 2. A model of angiogenesis is used to determine expression in angiogenesis

In the model of angiogenesis used to determine expression of angiogenesis-associated sequences, human umbilical vein endothelial cells (HUVEC) were obtained, *e.g.*, as passage 1 (p1) frozen cells from Cascade Biologics (Oregon) and grown in maintenance medium: Medium 199 (Life Technologies) supplemented with 20% pooled human serum, 100 mg/ml heparin and 75 mg/ml endothelial cell growth supplements (Sigma) and gentamicin (Life Technologies). An *in vitro* cell system model was used in which $2x10^5$ HUVECs were cultured in 0.5 ml 3 mgs/ml plasminogen-depleted fibrinogen (Calbiochem, San Diego, CA) that was polymerized by the addition of 1 unit of maintenance medium

supplemented with 100 ng/ml VEGF and HGF and 10 ng/ml TGF-a (R&D Systems, Minneapolis,MN) added (growth medium). The growth medium was replaced every 2 days. Samples for RNA were collected, *e.g.*, at 0, 2, 6, 15, 24, 48, and 96 hours of culture. The fibrin clots were placed in Trizol (Life Technologies) and disrupted using a Tissuemizer. Thereafter standard procedures were used for extracting the RNA (*e.g.*, Example 1).

Angiogenesis associated sequences thus identified are shown in Table 1. As indicated, some of the Accession numbers include expression sequence tags (ESTs). Thus, in one embodiment herein, genes within an expression profile, also termed expression profile genes, include ESTs and are not necessarily full length.

Table 1

AAA4 DNA sequence
Gene name: CGI-100 protein
Unigene number: Hs.275253
Probeset Accession #: AA089688
Nucleic Acid Accession #: NM_016040 cluster
Coding sequence: 142-831 (predicted start/stop codons underlined)

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GTTCGCCGCC GCCGCGCCGG CCACCTGGAG TTTTTTCAGA CTCCAGATTT CCCTGTCAAC    60
CACGAGGAGT CCAGAGAGGA AACGCGGAGC GGAGACAACA GTACCTGACG CCTCTTTCAG   120
CCCGGGATCG CCCCAGCAGG GATGGGCGAC AAGATCTGGC TGCCCTTCCC CGTGCTCCTT   180
CTGGCCGCTC TGCCTCCGGT GCTGCTGCCT GGGGCGGCCG GCTTCACACC TTCCCTCGAT   240
AGCGACTTCA CCTTTACCCT TCCCGCCGGC CAGAAGGAGT GCTTCTACCA GCCCATGCCC   300
CTGAAGGCCT CGCTGGAGAT CGAGTACCAA GTTTTAGATG GAGCAGGATT AGATATTGAT   360
TTCCATCTTG CCTCTCCAGA AGGCAAAACC TTAGTTTTTG AACAAAGAAA ATCAGATGGA   420
GTTCACACTG TAGAGACTGA AGTTGGTGAT TACATGTTCT GCTTTGACAA TACATTCAGC   480
ACCATTTCTG AGAAGGTGAT TTTCTTTGAA TTAATCCTGG ATAATATGGG AGAACAGGCA   540
CAAGAACAAG AAGATTGGAA GAAATATATT ACTGGCACAG ATATATTGGA TATGAAACTG   600
GAAGACATCC TGGAATCCAT CAACAGCATC AAGTCCAGAC TAAGCAAAAG TGGGCACATA   660
CAAACTCTGC TTAGAGCATT TGAAGCTCGT GATCGAAACA TACAAGAAAG CAACTTTGAT   720
AGAGTCAATT TCTGGTCTAT GGTTAATTTA GTGGTCATGG TGGTGGTGTC AGCCATTCAA   780
GTTTATATGC TGAAGAGTCT GTTTGAAGAT AAGAGGAAAA GTAGAACTTA AAACTCCAAA   840
CTAGAGTACG TAACATTGAA AAATGAGGCA TAAAAATGCA ATAAACTGTT ACAGTCAAGA   900
CCATTAATGG TCTTCTCCAA AATATTTTGA GATATAAAAG TAGGAAACAG GTATAATTTT   960
AATGTGAAAA TTAAGTCTTC ACTTTCTGTG CAAGTAATCC TGCTGATCCA GTTGTACTTA  1020
AGTGTGTAAC AGGAATATTT TGCAGAATAT AGGTTTAACT GAATGAAGCC ATATTAATAA  1080
CTGCATTTTC CTAACTTTGA AAAATTTTGC AAATGTCTTA GGTGATTTAA ATAAATGAGT  1140
ATTGGGCCTA AA
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AAA7 DNA sequence
Gene name: Endothelial differentiation, sphingolipid G-protein-coupled receptor, 1 (EDG1)
Unigene number: Hs.154210
Probeset Accession #: M31210
Nucleic Acid Accession #: NM_001400 cluster
Coding sequence: 251-1396 (predicted start/stop codons underlined)

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TCTAAAGGTC GGGGGCAGCA GCAAGATGCG AAGCGAGCCG TACAGATCCC GGGCTCTCCG    60
AACGCAACTT CGCCCTGCTT GAGCGAGGCT GCGGTTTCCG AGGCCCTCTC CAGCCAAGGA   120
AAAGCTACAC AAAAAGCCTG GATCACTCAT CGAACCACCC CTGAAGCCAG TGAAGGCTCT   180
CTCGCCTCGC CCTCTAGCGT TCGTCTGGAG TAGCGCCACC CCGGCTTCCT GGGGACACAG   240
GGTTGGCACC ATGGGGCCCA CCAGCGTCCC GCTGGTCAAG GCCCACCGCA GCTCGGTCTC   300
TGACTACGTC AACTATGATA TCATCGTCCG GCATTACAAC TACACGGGAA AGCTGAATAT   360
CAGCGCGGAC AAGGAGAACA GCATTAAACT GACCTCGGTG GTGTTCATTC TCATCTGCTG   420
CTTTATCATC CTGGAGAACA TCTTTGTCTT GCTGACCATT TGGAAAACCA AGAAATTCCA   480
CCGACCCATG TACTATTTTA TTGGCAATCT GGCCCTCTCA GACCTGTTGG CAGGAGTAGC   540
CTACACAGCT AACCTGCTCT TGTCTGGGGC CACCACCTAC AAGCTCACTC CCGCCCAGTG   600
GTTTCTGCGG GAAGGGAGTA TGTTTGTGGC CCTGTCAGCC TCCGTGTTCA GTCTCCTCGC   660
CATCGCCATT GAGCGCTATA TCACAATGCT GAAAATGAAA CTCCACAACG GGAGCAATAA   720
CTTCCGCCTC TTCCTGCTAA TCAGCGCCTG CTGGGTCATC TCCCTCATCC TGGGTGGCCT   780
GCCTATCATG GGCTGGAACT GCATCAGTGC GCTGTCCAGC TGCTCCACCG TGCTGCCGCT   840
CTACCACAAG CACTATATCC TCTTCTGCAC CACGGTCTTC ACTCTGCTTC TGCTCTCCAT   900
CGTCATTCTG TACTGCAGAA TCTACTCCTT GGTCAGGACT CGGAGCCGCC GCCTGACGTT   960
CCGCAAGAAC ATTTCCAAGG CCAGCCGCAG CTCTGAGAAT GTGGCGCTGC TCAAGACCGT  1020
AATTATCGTC CTGAGCGTCT TCATCGCCTG CTGGGCACCG CTCTTCATCC TGCTCCTGCT  1080
GGATGTGGGC TGCAAGGTGA AGACCTGTGA CATCCTCTTC AGAGCGGAGT ACTTCCTGGT  1140
GTTACCTGTG CTCAACTCCG GCACCAACCC CATCATTTAC ACTCTGACCA ACAAGGAGAT  1200
GCGTTCGGCC TTCATCCGGA TCATGTCCTG CTGCAAGTGC CCGAGCGGAG ACTCTGCTGG  1260
CAAATTCAAG CGACCCATCA TCGCCGGCAT GGAATTCAGC CGCAGCAAAT CGGACAATTC  1320
CTCCCACCCC CAGAAAGACG AAGGGGACAA CCCAGAGACC ATTATGTCTT CTGGAAACGT  1380
CAACTCTTCT TCCTAGAACT GGAAGCTGTC CACCCACCGG AAGCGCTCTT TACTTGGTCG  1440
CTGGCCACCC CAGTGTTTGG AAAAAAATCT CTGGGCTTCG ACTGCTGCCA GGGAGGAGCT  1500
GCTGCAAGCC AGAGGGAGGA AGGGGGAGAA TACGAACAGC CTGGTGGTGT CGGGTGTTGG  1560
TGGGTAGAGT TAGTTCCTGT GAACAATGCA CTGGGAAGGG TGGAGATCAG GTCCCGGCCT  1620
GGAATATATA TTCTACCCCC CTGGAGCTTT GATTTTGCAC TGAGCCAAAG GTCTAGCATT  1680
GTCAAGCTCC TAAAGGGTTC ATTTGGCCCC TCCTCAAAGA CTAATGTCCC CATGTGAAAG  1740
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CGTCTCTTTG TCTGGAGCTT TGAGGAGATG TTTTCCTTCA CTTTAGTTTC AAACCCAAGT 1800
GAGTGTGTGC ACTTCTGCTT CTTTAGGGAT GCCCTGTACA TCCCACACCC CACCCTCCCT 1860
TCCCTTCATA CCCCTCCTCA ACGTTCTTTT ACTTTATACT TTAACTACCT GAGAGTTATC 1920
AGAGCTGGGG TTGTGGAATG ATCGATCATC TATAGCAAAT AGGCTATGTT GAGTACGTAG 1980
GCTGTGGGAA GATGAAGATG GTTTGGAGGT GTAAAACAAT GTCCTTCGCT GAGGCCAAAG 2040
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AAAACATCTT TTCAATGAAA TGTGTTACCA TTTCATATCC ATTGAAGCCG AAATCTGCAT 2160
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GACAAGCAAA ACAAAGTGAA AACCGAATGG ATTAACTTTT GCAAACCAAG GGAGATTTCT 2280
TAGCAAATGA GTCTAACAAA TATGACATCC GTCTTTCCCA CTTTTGTTGA TGTTTATTTC 2340
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TTTTCTTGAT TTTTGAATGT ATTTGTTTCA GGAAGAAGTC ATTTTATGGA TTTTTCTAAC 2460
CCGTGTTAAC TTTTCTAGAA TCCACCCTCT TGTGCCCTTA AGCATTACTT TAACTGGTAG 2520
GGAACGCCAG AACTTTTAAG TCCAGCTATT CATTAGATAG TAATTGAAGA TATGTATAAA 2580
TATTACAAAG AATAAAAATA TATTACTGTC TCTTTAGTAT GGTTTTCAGT GCAATTAAAC 2640
CGAGAGATGT CTTGTTTTTT TAAAAAGAAT AGTATTTAAT AGGTTTCTGA CTTTTGTGGA 2700
TCATTTTGCA CATAGCTTTA TCAACTTTTA AACATTAATA AACTGATTTT TTTAAAG

AAB3 DNA sequence
Gene name: Solute carrier family 20 (phosphate transporter), member 1, Human leukaemia virus receptor 1 (GLVR1)
Unigene number: Hs.78452
Probeset Accession #: L20859
Nucleic Acid Accession #: NM_005415 cluster
Coding sequence: predicted 371-2410 (predicted start/stop codons underlined)

GAGCTGTCCC CGGTGCCGCC GACCCGGGCC GTGCCGTGTG CCCGTGGCTC CAGCCGCTGC 60
CGCCTCGATC TCCTCGTCTC CCGCTCCGCC CTCCCTTTTC CCTGGATGAA CTTGCGTCCT 120
TTCTCTTCTC CGCCATGGAA TTCTGCTCCG TGCTTTTAGC CCTCCTGAGC CAAAGAAACC 180
CCAGACAACA GATGCCCATA CGCAGCGTAT AGCAGTAACT CCCCAGCTCG GTTTCTGTGC 240
CGTAGTTTAC AGTATTTAAT TTTATATAAT ATATATTATT TATTATAGCA TTTTTGATAC 300
CTCATATTCT GTTTACACAT CTTGAAAGGC GCTCAGTAGT TCTCTTACTA AACAACCACT 360
ACTCCAGAGA ATGGCAACGC TGATTACCAG TACTACAGCT GCTACCGCCG CTTCTGGTCC 420
TTTGGTGGAC TACCTATGGA TGCTCATCCT GGGCTTCATT ATTGCATTTG TCTTGGCATT 480
CTCCGTGGGA GCCAATGATG TAGCAAATTC TTTTGGTACA GCTGTGGGCT CAGGTGTAGT 540
GACCCTGAAG CAAGCCTGCA TCCTAGCTAG CATCTTTGAA ACAGTGGGCT CTGTCTTACT 600
GGGGGCCAAA GTGAGCGAAA CCATCCGGAA GGGCTTGATT GACGTGGAGA TGTACAACTC 660
GACTCAAGGG CTACTGATGG CCGGCTCAGT CAGTGCTATG TTTGGTTCTG CTGTGTGGCA 720
ACTCGTGGCT TCGTTTTTGA AGCTCCCTAT TTCTGGAACC CATTGTATTG TTGGTGCAAC 780
TATTGGTTTC TCCCTCGTGG CAAAGGGGCA GGAGGGTGTC AAGTGGTCTG AACTGATAAA 840
AATTGTGATG TCTTGGTTCG TGTCCCCACT GCTTTCTGGA ATTATGTCTG GAATTTTATT 900
CTTCCTGGTT CGTGCATTCA TCCTCCATAA GGCAGATCCA GTTCCTAATG GTTTGCGAGC 960
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AGCACCGTTG CTGGGCTTTG ACAAACTTCC TCTGTGGGGT ACCATCCTCA TCTCGGTGGG 1080
ATGTGCAGTT TTCTGTGCCC TTATCGTCTG GTTCTTTGTA TGTCCCAGGA TGAAGAGAAA 1140
AATTGAACGA GAAATAAAGT GTAGTCCTTC TGAAAGCCCC TTAATGGAAA AAAAGAATAG 1200
CTTGAAAGAA GACCATGAAG AAACAAAGTT GTCTGTTGGT GATATTGAAA ACAAGCATCC 1260
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CTCATTCAAA CTTGGAGATT TGGAGGAAGC TCCAGAGAGA GAGAGGCTTC CCAGCGTGGA 1380
CTTGAAAGAG GAAACCAGCA TAGATAGCAC CGTGAATGGT GCAGTGCAGT TGCCTAATGG 1440
GAACCTTGTC CAGTTCAGTC AAGCCGTCAG CAACCAAATA AACTCCAGTG GCCACTCCCA 1500
GTATCACACC GTGCATAAGG ATTCCGGCCT GTACAAAGAG CTACTCCATA AATTACATCT 1560
TGCCAAGGTG GGAGATTGCA TGGGAGACTC CGGTGACAAA CCCTTAAGGC GCAATAATAG 1620
CTATACTTCC TATACCATGG CAATATGTGG CATGCCTCTG GATTCATTCC GTGCCAAAGA 1680
AGGTGAACAG AAGGGCGAAG AAATGGAGAA GCTGACATGG CCTAATGCAG ACTCCAAGAA 1740
GCGAATTCGA ATGGACAGTT ACACCAGTTA CTGCAATGCT GTGTCTGACC TTCACTCAGC 1800
ATCTGAGATA GACATGAGTG TCAAGGCAGC GATGGGTCTA GGTGACAGAA AAGGAAGTAA 1860
TGGCTCTCTA GAAGAATGGT ATGACCAGGA TAAGCCTGAA GTCTCTCTCC TCTTCCAGTT 1920
CCTGCAGATC CTTACAGCCT GCTTTTGGTC ATTCGCCCAT GGTGGCAATG ACGTAAGCAA 1980
TGCCATTGGG CCTCTGGTTG CTTTATATTT GGTTTATGAC ACAGGAGATG TTTCTTCAAA 2040
AGTGGCAACA CCAATATGGC TTCTACTCTA TGGTGGTGTT GGTATCTGTG TTGGTCTGTG 2100
GGTTTGGGGA AGAAGAGTTA TCCAGACCAT GGGGAAGGAT CTGACACCGA TCACACCCTC 2160
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CCTTCCCATC AGTACAACAC ATTGTAAAGT GGGCTCTGTT GTGTCTGTTG GCTGGCTCCG 2280
GTCCAAGAAG GCTGTTGACT GGCGTCTCTT TCGTAACATT TTTATGGCCT GGTTTGTCAC 2340
AGTCCCCATT TCTGGAGTTA TCAGTGCTGC CATCATGGCA ATCTTCAGAT ATGTCATCCT 2400
CAGAATGTGA AGCTGTTTGA GATTAAAATT TGTGTCAATG TTTGGGACCA TCTTAGGTAT 2460

TCCTGCTCCC CTGAAGAATG ATTACAGTGT TAACAGAAGA CTGACAAGAG TCTTTTTATT 2520
TGGGAGCAGA GGAGGGAAGT GTTACTTGTG CTATAACTGC TTTTGTGCTA AATATGAATT 2580
GTCTCAAAAT TAGCTGTGTA AAATAGCCCG GGTTCCACTG GCTCCTGCTG AGGTCCCCTT 2640
TCCTTCTGGG CTGTGAATTC CTGTACATAT TTCTCTACTT TTTGTATCAG GCTTCAATTC 2700
CATTATGTTT TAATGTTGTC TCTGAAGATG ACTTGTGATT TTTTTTTCTT TTTTTTAAAC 2760
CATGAAGAGC CGTTTGACAG AGCATGCTCT GCGTTGTTGG TTTCACCAGC TTCTGCCCTC 2820
ACATGCACAG GGATTTAACA ACAAAAATAT AACTACAACT TCCCTTGTAG TCTCTTATAT 2880
AAGTAGAGTC CTTGGTACTC TGCCCTCCTG TCAGTAGTGG CAGGATCTAT TGGCATATTC 2940
GGGAGCTTCT TAGAGGGATG AGGTTCTTTG AACACAGTGA AAATTTAAAT TAGTAACTTT 3000
TTTGCAAGCA GTTTATTGAC TGTTATTGCT AAGAAGAAGT AAGAAAGAAA AAGCCTGTTG 3060
GCAATCTTGG TTATTTCTTT AAGATTTCTG GCAGTGTGGG ATGGATGAAT GAAGTGGAAT 3120
GTGAACTTTG GGCAAGTTAA ATGGGACAGC CTTCCATGTT CATTTGTCTA CCTCTTAACT 3180
GAATAAAAAA GCCTACAGTT TTTAGAAAAA ACCCGAATTC

AAB4 DNA sequence
Gene name: Matrix metalloproteinase 10 (stromelysin 2)
Unigene number: Hs.2258
Probeset Accession #: X07820
Nucleic Acid Accession #: NM_002425
Coding sequence: predicted 23-1453 (predicted start/stop codons underlined)

AAAGAAGGTA AGGGCAGTGA GAATGATGCA TCTTGCATTC CTTGTGCTGT TGTGTCTGCC 60
AGTCTGCTCT GCCTATCCTC TGAGTGGGGC AGCAAAAGAG GAGGACTCCA ACAAGGATCT 120
TGCCCAGCAA TACCTAGAAA AGTACTACAA CCTCGAAAAG GATGTGAAAC AGTTTAGAAG 180
AAAGGACAGT AATCTCATTG TTAAAAAAAT CCAAGGAATG CAGAAGTTCC TTGGGTTGGA 240
GGTGACAGGG AAGCTAGACA CTGACACTCT GGAGGTGATG CGCAAGCCCA GGTGTGGAGT 300
TCCTGACGTT GGTCACTTCA GCTCCTTTCC TGGCATGCCG AAGTGGAGGA AAACCCACCT 360
TACATACAGG ATTGTGAATT ATACACCAGA TTTGCCAAGA GATGCTGTTG ATTCTGCCAT 420
TGAGAAAGCT CTGAAAGTCT GGGAAGAGGT GACTCCACTC ACATTCTCCA GGCTGTATGA 480
AGGAGAGGCT GATATAATGA TCTCTTTCGC AGTTAAAGAA CATGGAGACT TTTACTCTTT 540
TGATGGCCCA GGACACAGTT TGGCTCATGC CTACCCACCT GGACCTGGGC TTTATGGAGA 600
TATTCACTTT GATGATGATG AAAAATGGAC AGAAGATGCA TCAGGCACCA ATTTATTCCT 660
CGTTGCTGCT CATGAACTTG GCCACTCCCT GGGGCTCTTT CACTCAGCCA ACACTGAAGC 720
TTTGATGTAC CCACTCTACA ACTCATTCAC AGAGCTCGCC CAGTTCCGCC TTTCGCAAGA 780
TGATGTGAAT GGCATTCAGT CTCTCTACGG ACCTCCCCCT GCCTCTACTG AGGAACCCCT 840
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GTCCTTCGAT GCCATCAGCA CTCTGAGGGG AGAATATCTG TTCTTTAAAG ACAGATATTT 960
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CTCTCTTCCA TCATATTTGG ATGCTGCATA TGAAGTTAAC AGCAGGGACA CCGTTTTTAT 1080
TTTTAAAGGA AATGAGTTCT GGGCCATCAG AGGAAATGAG GTACAAGCAG GTTATCCAAG 1140
AGGCATCCAT ACCCTGGGTT TTCCTCCAAC CATAAGGAAA ATTGATGCAG CTGTTTCTGA 1200
CAAGGAAAAG AAGAAAACAT ACTTCTTTGC AGCGGACAAA TACTGGAGAT TTGATGAAAA 1260
TAGCCAGTCC ATGGAGCAAG GCTTCCCTAG ACTAATAGCT GATGACTTTC CAGGAGTTGA 1320
GCCTAAGGTT GATGCTGTAT TACAGGCATT TGGATTTTTC TACTTCTTCA GTGGATCATC 1380
ACAGTTTGAG TTTGACCCCA ATGCCAGGAT GGTGACACAC ATATTAAAGA GTAACAGCTG 1440
GTTACATTGC TAGGCGAGAT AGGGGGAAGA CAGATATGGG TGTTTTTAAT AAATCTAATA 1500
ATTATTCATC TAATGTATTA TGAGCCAAAA TGGTTAATTT TTCCTGCATG TTCTGTGACT 1560
GAAGAAGATG AGCCTTGCAG ATATCTGCAT GTGTCATGAA GAATGTTTCT GGAATTCTTC 1620
ACTTGCTTTT GAATTGCACT GAACAGAATT AAGAAATACT CATGTGCAAT AGGTGAGAGA 1680
ATGTATTTTC ATAGATGTGT TATTACTTCC TCAATAAAAA GTTTTATTTT GGGCCTGTTC 1740
CTT

AAB6 DNA sequence
Gene name: Podocalyxin-like
Unigene number: Hs.16426
Probeset Accession #: U97519
Nucleic Acid Accession #: NM_005397 cluster
Coding sequence: 251-1837 (predicted start/stop codons underlined)

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CAGCCCGGCT CTGCTGCAGC GGCAGGGAGG AAGAGCCGCC GCAGCGCGAC TCGGGAGCCC 120
CGGGCCACAG CCTGGCCTCC GGAGCCACCC ACAGGCCTCC CCGGGCGGCG CCCACGCTCC 180
TACCGCCCGG ACGCGCGGAT CCTCCGCCGG CACCGCAGCC ACCTGCTCCC GGCCCAGAGG 240
CGACGACACG ATGCGCTGCG CGCTGGCGCT CTCGGCGCTG CTGCTACTGT TGTCAACGCC 300
GCCGCTGCTG CCGTCGTCGC CGTCGCCGTC GCCGTCGCCG TCGCCCTCCC AGAATGCAAC 360
CCAGACTACT ACGGACTCAT CTAACAAAAC AGCACCGACT CCAGCATCCA GTGTCACCAT 420

CATGGCTACA GATACAGCCC AGCAGAGCAC AGTCCCCACT TCCAAGGCCA ACGAAATCTT 480
GGCCTCGGTC AAGGCGACCA CCCTTGGTGT ATCCAGTGAC TCACCGGGGA CTACAACCCT 540
GGCTCAGCAA GTCTCAGGCC CAGTCAACAC TACCGTGGCT AGAGGAGGCG GCTCAGGCAA 600
CCCTACTACC ACCATCGAGA GCCCCAAGAG CACAAAAAGT GCAGACACCA CTACAGTTGC 660
AACCTCCACA GCCACAGCTA AACCTAACAC CACAAGCAGC CAGAATGGAG CAGAAGATAC 720
AACAAACTCT GGGGGGAAAA GCAGCCACAG TGTGACCACA GACCTCACAT CCACTAAGGC 780
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GCATCCTGTG GCCACCCCAA CAAGCTCGGG ACATGACCAT CTTATGAAAA TTTCAAGCAG 900
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GATGGAGAAC AGTGCCTGTT TGGGGGAAAA CAGGAAATCT TGTTAGGCTT GAGTGAGGTG 3900
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ACTGTGGTTT CCCCAAGCTG CACAGGAGGC CAGAAACCAC AAGTATGATG ACTAGGAAGC 4560
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GACTGTGCGC CTCAGAAGGA ATAATCGGTA AATTAAGAAT TGCTACTCGA AGGTGCCAGA 5340
ATGACACAAA GGACAGAATT CCTTTCCCAG TTGTTACCCT AGCAAGGCTA GGGAGGGCAT 5400
GAACACAAAC ATAAGAACTG GTCTTCTCAC ACTTTCTCTG AATCATTTAG GTTTAAGATG 5460
TAAGTGAACA ATTCTTTCTT TCTGCCAAGA AACAAAGTTT TGGATGAGCT TTTATATATG 5520
GAACTTACTC CAACAGGACT GAGGGACCAA GGAAACATGA TGGGGGAGGC AAGAGAGGGC 5580
AAAGAGTAAA ACTGTAGCAT AGCTTTTGTC ACGGTCACTA GCTGATCCCT CAGGTCTGCT 5640
GCAAACACAG CATGGAGGAC ACAGATGACT CTTTGGTGTT GGTCTTTTTG TCTGCAGTGA 5700
ATGTTCAACA GTTTGCCCAG GAACTGGGGG ATCATATATG TCTTAGTGGA CAGGGGTCTG 5760
AAGTACACTG GAATTTACTG AGAAACTTGT TTGTAAAAAC TATAGTTAAT AATTATTGCA 5820
TTTTCTTACA AAAATATATT TTGGAAAATT GTATACTGTC AATTAAAGT

AAB8 DNA sequence
Gene name: EGF-containing fibulin-like extracellular matrix protein 1
Unigene number: Hs.76224
Probeset Accession #: U03877
Nucleic Acid Accession #: NM_004105 Transcript variant 1
Coding sequence: 150-1631 (predicted start/stop codons underlined)

CTAGTATTCT ACTAGAACTG GAAGATTGCT CTCCGAGTTT TTTTTTGTT ATTTTGTTAA 60
AAAATAAAAA GCTTGAGCAG CAATTCATAT TACTGTCACA GGTATTTTTG CTGTGCTGTG 120
CAAGGTAACT CTGCTAGCTA AGATTCACAA TGTTGAAAGC CCTTTTCCTA ACTATGCTGA 180
CTCTGGCGCT GGTCAAGTCA CAGGACACCG AAGAAACCAT CACGTACACG CAATGCACTG 240
ACGGATATGA GTGGGATCCT GTGAGACAGC AATGCAAAGA TATTGATGAA TGTGACATTG 300
TCCCAGACGC TTGTAAAGGT GGAATGAAGT GTGTCAACCA CTATGGAGGA TACCTCTGCC 360
TTCCGAAAAC AGCCCAGATT ATTGTCAATA ATGAACAGCC TCAGCAGGAA ACACAACCAG 420
CAGAAGGAAC CTCAGGGGCA ACCACCGGGG TTGTAGCTGC CAGCAGCATG GCAACCAGTG 480
GAGTGTTGCC CGGGGGTGGT TTTGTGGCCA GTGCTGCTGC AGTCGCAGGC CCTGAAATGC 540
AGACTGGCCG AAATAACTTT GTCATCCGGC GGAACCCAGC TGACCCTCAG CGCATTCCCT 600
CCAACCCTTC CCACCGTATC CAGTGTGCAG CAGGCTACGA GCAAAGTGAA CACAACGTGT 660
GCCAAGACAT AGACGAGTGC ACTGCAGGGA CGCACAACTG TAGAGCAGAC CAAGTGTGCA 720
TCAATTTACG GGGATCCTTT GCATGTCAGT GCCCTCCTGG ATATCAGAAG CGAGGGGAGC 780
AGTGCGTAGA CATAGATGAA TGTACCATCC CTCCATATTG CCACCAAAGA TGCGTGAATA 840
CACCAGGCTC ATTTTATTGC CAGTGCAGTC CTGGGTTTCA ATTGGCAGCA AACAACTATA 900
CCTGCGTAGA TATAAATGAA TGTGATGCCA GCAATCAATG TGCTCAGCAG TGCTACAACA 960
TTCTTGGTTC ATTCATCTGT CAGTGCAATC AAGGATATGA GCTAAGCAGT GACAGGCTCA 1020
ACTGTGAAGA CATTGATGAA TGCAGAACCT CAAGCTACCT GTGTCAATAT CAATGTGTCA 1080
ATGAACCTGG GAAATTCTCA TGTATGTGCC CCCAGGGATA CCAAGTGGTG AGAAGTAGAA 1140
CATGTCAAGA TATAAATGAG TGTGAGACCA CAAATGAATG CCGGGAGGAT GAAATGTGTT 1200
GGAATTATCA TGGCGGCTTC CGTTGTTATC CACGAAATCC TTGTCAAGAT CCCTACATTC 1260
TAACACCAGA GAACCGATGT GTTTGCCCAG TCTCAAATGC CATGTGCCGA GAACTGCCCC 1320
AGTCAATAGT CTACAAATAC ATGAGCATCC GATCTGATAG GTCTGTGCCA TCAGACATCT 1380
TCCAGATACA GGCCACAACT ATTTATGCCA ACACCATCAA TACTTTTCGG ATTAAATCTG 1440
GAAATGAAAA TGGAGAGTTC TACCTACGAC AAACAAGTCC TGTAAGTGCA ATGCTTGTGC 1500
TCGTGAAGTC ATTATCAGGA CCAAGAGAAC ATATCGTGGA CCTGGAGATG CTGACAGTCA 1560
GCAGTATAGG GACCTTCCGC ACAAGCTCTG TGTTAAGATT GACAATAATA GTGGGGCCAT 1620
TTTCATTTTA GTCTTTTCTA AGAGTCAACC ACAGGCATTT AAGTCAGCCA AAGAATATTG 1680
TTACCTTAAA GCACTATTTT ATTTATAGAT ATATCTAGTG CATCTACATC TCTATACTGT 1740
ACACTCACCC ATAACAAACA ATTACACCAT GGTATAAAGT GGGCATTTAA TATGTAAAGA 1800
TTCAAAGTTT GTCTTTATTA CTATATGTAA ATTAGACATT AATCCACTAA ACTGGTCTTC 1860
TTCAAGAGAG CTAAGTATAC ACTATCTGGT GAAACTTGGA TTCTTTCCTA TAAAAGTGGG 1920
ACCAAGCAAT GATGATCTTC TGTGGTGCTT AAGGAAACTT ACTAGAGCTC CACTAACAGT 1980
CTCATAAGGA GGCAGCCATC ATAACCATTG AATAGCATGC AAGGGTAAGA ATGAGTTTTT 2040
AACTGCTTTG TAAGAAAATG GAAAAGGTCA ATAAAGATAT ATTTCTTTAG AAAATGGGGA 2100
TCTGCCATAT TTGTGTTGGT TTTTATTTTC ATATCCAGCC TAAAGGTGGT TGTTTATTAT 2160

ATAGTAATAA ATCATTGCTG TACAACATGC TGGTTTCTGT AGGGTATTTT TAATTTTGTC 2220
AGAAATTTTA GATTGTGAAT ATTTTGTAAA AAACAGTAAG CAAAATTTTC CAGAATTCCC 2280
AAAATGAACC AGATACCCCC TAGAAAATTA TACTATTGAG AAATCTATGG GGAGGATATG 2340
AGAAAATAAA TTCCTTCTAA ACCACATTGG AACTGACCTG AAGAAGCAAA CTCGGAAAAT 2400
ATAATAACAT CCCTGAATTC AGGCATTCAC AAGATGCAGA ACAAAATGGA TAAAAGGTAT 2460
TTCACTGGAG AAGTTTTAAT TTCTAAGTAA AATTTAAATC CTAACACTTC ACTAATTTAT 2520
AACTAAAATT TCTCATCTTC GTACTTGATG CTCACAGAGG AAGAAAATGA TGATGGTTTT 2580
TATTCCTGGC ATCCAGAGTG ACAGTGAACT TAAGCAAATT ACCCTCCTAC CCAATTCTAT 2640
GGAATATTTT ATACGTCTCC TTGTTTAAAA TCTGACTGCT TTACTTTGAT GTATCATATT 2700
TTTAAATAAA AATAAATATT CCTTTAGAAG ATCACTCTAA AA

AAB9 DNA sequence
Gene name: Melanoma adhesion molecule, MUC 18 glycoprotein
Unigene number: Hs.211579
Probeset Accession #: M28882
Nucleic Acid Accession #: NM_006500 cluster
Coding sequence: 27-1967 (predicted start/stop codons underlined)

ACTTGCGTCT CGCCCTCCGG CCAAGCATGG GGCTTCCCAG GCTGGTCTGC GCCTTCTTGC 60
TCGCCGCCTG CTGCTGCTGT CCTCGCGTCG CGGGTGTGCC CGGAGAGGCT GAGCAGCCTG 120
CGCCTGAGCT GGTGGAGGTG GAAGTGGGCA GCACAGCCCT TCTGAAGTGC GGCCTCTCCC 180
AGTCCCAAGG CAACCTCAGC CATGTCGACT GGTTTTCTGT CCACAAGGAG AAGCGGACGC 240
TCATCTTCCG TGTGCGCCAG GGCCAGGGCC AGAGCGAACC TGGGGAGTAC GAGCAGCGGC 300
TCAGCCTCCA GGACAGAGGG GCTACTCTGG CCCTGACTCA AGTCACCCCC CAAGACGAGC 360
GCATCTTCTT GTGCCAGGGC AAGCGCCCTC GGTCCCAGGA GTACCGCATC CAGCTCCGCG 420
TCTACAAAGC TCCGGAGGAG CCAAACATCC AGGTCAACCC CCTGGGCATC CCTGTGAACA 480
GTAAGGAGCC TGAGGAGGTC GCTACCTGTG TAGGGAGGAA CGGGTACCCC ATTCCTCAAG 540
TCATCTGGTA CAAGAATGGC CGGCCTCTGA AGGAGGAGAA GAACCGGGTC CACATTCAGT 600
CGTCCCAGAC TGTGGAGTCG AGTGGTTTGT ACACCTTGCA GAGTATTCTG AAGGCACAGC 660
TGGTTAAAGA AGACAAAGAT GCCCAGTTTT ACTGTGAGCT CAACTACCGG CTGCCCAGTG 720
GGAACCACAT GAAGGAGTCC AGGGAAGTCA CCGTCCCTGT TTTCTACCCG ACAGAAAAAG 780
TGTGGCTGGA AGTGGAGCCC GTGGGAATGC TGAAGGAAGG GGACCGCGTG GAAATCAGGT 840
GTTTGGCTGA TGGCAACCCT CCACCACACT TCAGCATCAG CAAGCAGAAC CCCAGCACCA 900
GGGAGGCAGA GGAAGAGACA ACCAACGACA ACGGGGTCCT GGTGCTGGAG CCTGCCCGGA 960
AGGAACACAG TGGGCGCTAT GAATGTCAGG CCTGGAACTT GGACACCATG ATATCGCTGC 1020
TGAGTGAACC ACAGGAACTA CTGGTGAACT ATGTGTCTGA CGTCCGAGTG AGTCCCGCAG 1080
CCCCTGAGAG ACAGGAAGGC AGCAGCCTCA CCCTGACCTG TGAGGCAGAG AGTAGCCAGG 1140
ACCTCGAGTT CCAGTGGCTG AGAGAAGAGA CAGACCAGGT GCTGGAAAGG GGGCCTGTGC 1200
TTCAGTTGCA TGACCTGAAA CGGGAGGCAG GAGGCGGCTA TCGCTGCGTG GCGTCTGTGC 1260
CCAGCATACC CGGCCTGAAC CGCACACAGC TGGTCAAGCT GGCCATTTTT GGCCCCCCTT 1320
GGATGGCATT CAAGGAGAGG AAGGTGTGGG TGAAAGAGAA TATGGTGTTG AATCTGTCTT 1380
GTGAAGCGTC AGGGCACCCC CGGCCCACCA TCTCCTGGAA CGTCAACGGC ACGGCAAGTG 1440
AACAAGACCA AGATCCACAG CGAGTCCTGA GCACCCTGAA TGTCCTCGTG ACCCCGGAGC 1500
TGTTGGAGAC AGGTGTTGAA TGCACGGCCT CCAACGACCT GGGCAAAAAC ACCAGCATCC 1560
TCTTCCTGGA GCTGGTCAAT TTAACCACCC TCACACCAGA CTCCAACACA ACCACTGGCC 1620
TCAGCACTTC CACTGCCAGT CCTCATACCA GAGCCAACAG CACCTCCACA GAGAGAAAGC 1680
TGCCGGAGCC GGAGAGCCGG GGCGTGGTCA TCGTGGCTGT GATTGTGTGC ATCCTGGTCC 1740
TGGCGGTGCT GGGCGCTGTC CTCTATTTCC TCTATAAGAA GGGCAAGCTG CCGTGCAGGC 1800
GCTCAGGGAA GCAGGAGATC ACGCTGCCCC CGTCTCGTAA GACCGAACTT GTAGTTGAAG 1860
TTAAGTCAGA TAAGCTCCCA GAAGAGATGG GCCTCCTGCA GGGCAGCAGC GGTGACAAGA 1920
GGGCTCCGGG AGACCAGGGA GAGAAATACA TCGATCTGAG GCATTAGCCC CGAATCACTT 1980
CAGCTCCCTT CCCTGCCTGG ACCATTCCCA GCTCCCTGCT CACTCTTCTC TCAGCCAAAG 2040
CCTCCAAAGG GACTAGAGAG AAGCCTCCTG CTCCCCTCAC CTGCACACCC CCTTTCAGAG 2100
GGCCACTGGG TTAGGACCTG AGGACCTCAC TTGGCCCTGC AAGCCGCTTT TCAGGGACCA 2160
GTCCACCACC ATCTCCTCCA CGTTGAGTGA AGCTCATCCC AAGCAAGGAG CCCCAGTCTC 2220
CCGAGCGGGT AGGAGAGTTT CTTGCAGAAC GTGTTTTTTC TTTACACACA TTATGGCTGT 2280
AAATACCTGG CTCCTGCCAG CAGCTGAGCT GGGTAGCCTC TCTGAGCTGG TTTCCTGCCC 2340
CAAAGGCTGG CTTCCACCAT CCAGGTGCAC CACTGAAGTG AGGACACACC GGAGCCAGGC 2400
GCCTGCTCAT GTTGAAGTGC GCTGTTCACA CCCGCTCCGG AGAGCACCCC AGCGGCATCC 2460
AGAAGCAGCT GCAGTGTTGC TGCCACCACC CTCCTGCTCG CCTCTTCAAA GTCTCCTGTG 2520
ACATTTTTTC TTTGGTCAGA AGCCAGGAAC TGGTGTCATT CCTTAAAAGA TACGTGCCGG 2580
GGCCAGGTGT GGTGGCTCAC GCCTGTAATC CCAGCACTTT GGGAGGCCGA GGCGGGCGGA 2640
TCACAAAGTC AGGACGAGAC CATCCTGGCT AACACGGTGA AACCCTGTCT CTACTAAAAA 2700
TACAAAAAAA AATTAGCTAG GCGTAGTGGT TGGCACCTAT AGTCCCAGCT ACTCGGAAGG 2760
CTGAAGCAGG AGAATGGTAT GAATCCAGGA GGTGGAGCTT GCAGTGAGCC GAGACCGTGC 2820
CACTGCACTC CAGCCTGGGC AACACAGCGA GACTCCGTCT CGAGGAAAAA AAAAGAAAAG 2880
ACGCGTACCT GCGGTGAGGA AGCTGGGCGC TGTTTTCGAG TTCAGGTGAA TTAGCCTCAA 2940

TCCCCGTGTT CACTTGCTCC CATAGCCCTC TTGATGGATC ACGTAAAACT GAAAGGCAGC 3000
GGGGAGCAGA CAAAGATGAG GTCTACACTG TCCTTCATGG GGATTAAAGC TATGGTTATA 3060
TTAGCACCAA ACTTCTACAA ACCAAGCTCA GGGCCCCAAC CCTAGAAGGG CCCAAATGAG 3120
AGAATGGTAC TTAGGGATGG AAAACGGGGC CTGGCTAGAG CTTCGGGTGT GTGTGTCTGT 3180
CTGTGTGTAT GCATACATAT GTGTGTATAT ATGGTTTTGT CAGGTGTGTA AATTTGCAAA 3240
TTGTTTCCTT TATATATGTA TGTATATATA TATATGAAAA TATATATATA TATGAAAAAT 3300
AAAGCTTAAT TGTCCCAGAA AATCATACAT TGCTTTTTTA TTCTACATGG GTACCACAGG 3360
AACCTGGGGG CCTGTGAAAC TACAACCAAA AGGCACACAA AACCGTTTCC AGTTGGCAGC 3420
AGAGATCAGG GGTTACCTCT GCTTCTGAGC AAATGGCTCA AGCTCTACCA GAGCAGACAG 3480
CTACCCTACT TTTCAGCAGC AAAACGTCCC GTATGACGCA GCACGAAGGG CCTGGCAGGC 3540
TGTTAGCAGG AGCTATGTCC CTTCCTATCG TTTCCGTCCA CTT

AAC1 DNA sequence
Gene name: Matrix metalloproteinase 1 (interstitial collagenase)
Unigene number: Hs.83169
Probeset Accession #: X54925
Nucleic Acid Accession #: NM_002421 cluster
Coding sequence: 69-1478 (predicted start/stop codons underlined)

ATATTGGAGT AGCAAGAGGC TGGGAAGCCA TCACTTACCT TGCACTGAGA AAGAAGACAA 60
AGGCCAGTAT GCACAGCTTT CCTCCACTGC TGCTGCTGCT GTTCTGGGGT GTGGTGTCTC 120
ACAGCTTCCC AGCGACTCTA GAAACACAAG AGCAAGATGT GGACTTAGTC CAGAAATACC 180
TGGAAAAATA CTACAACCTG AAGAATGATG GGAGGCAAGT TGAAAAGCGG AGAAATAGTG 240
GCCCAGTGGT TGAAAAATTG AAGCAAATGC AGGAATTCTT TGGGCTGAAA GTGACTGGGA 300
AACCAGATGC TGAAACCCTG AAGGTGATGA AGCAGCCCAG ATGTGGAGTG CCTGATGTGG 360
CTCAGTTTGT CCTCACTGAG GGGAACCCTC GCTGGGAGCA AACACATCTG ACCTACAGGA 420
TTGAAAATTA CACGCCAGAT TTGCCAAGAG CAGATGTGGA CCATGCCATT GAGAAAGCCT 480
TCCAACTCTG GAGTAATGTC ACACCTCTGA CATTCACCAA GGTCTCTGAG GGTCAAGCAG 540
ACATCATGAT ATCTTTTGTC AGGGGAGATC ATCGGGACAA CTCTCCTTTT GATGGACCTG 600
GAGGAAATCT TGCTCATGCT TTTCAACCAG GCCCAGGTAT TGGAGGGGAT GCTCATTTTG 660
ATGAAGATGA AAGGTGGACC AACAATTTCA GAGAGTACAA CTTACATCGT GTTGCGGCTC 720
ATGAACTCGG CCATTCTCTT GGACTCTCCC ATTCTACTGA TATCGGGGCT TTGATGTACC 780
CTAGCTACAC CTTCAGTGGT GATGTTCAGC TAGCTCAGGA TGACATTGAT GGCATCCAAG 840
CCATATATGG ACGTTCCCAA AATCCTGTCC AGCCCATCGG CCCACAAACC CCAAAAGCAT 900
GTGACAGTAA GCTAACCTTT GATGCTATAA CTACGATTCG GGGAGAAGTG ATGTTCTTTA 960
AAGACAGATT CTACATGCGC ACAAATCCCT TCTACCCGGA AGTTGAGCTC AATTTCATTT 1020
CTGTTTTCTG GCCACAACTG CCAAATGGGC TTGAAGCTGC TTACGAATTT GCCGACAGAG 1080
ATGAAGTCCG GTTTTTCAAA GGGAATAAGT ACTGGGCTGT TCAGGGACAG AATGTGCTAC 1140
ACGGATACCC CAAGGACATC TACAGCTCCT TTGGCTTCCC TAGAACTGTG AAGCATATCG 1200
ATGCTGCTCT TTCTGAGGAA AACACTGGAA AAACCTACTT CTTTGTTGCT AACAAATACT 1260
GGAGGTATGA TGAATATAAA CGATCTATGG ATCCAGGTTA TCCCAAAATG ATAGCACATG 1320
ACTTTCCTGG AATTGGCCAC AAAGTTGATG CAGTTTTCAT GAAAGATGGA TTTTTCTATT 1380
TCTTTCATGG AACAAGACAA TACAAATTTG ATCCTAAAAC GAAGAGAATT TTGACTCTCC 1440
AGAAAGCTAA TAGCTGGTTC AACTGCAGGA AAAATTGAAC ATTACTAATT TGAATGGAAA 1500
ACACATGGTG TGAGTCCAAA GAAGGTGTTT TCCTGAAGAA CTGTCTATTT TCTCAGTCAT 1560
TTTTAACCTC TAGAGTCACT GATACACAGA ATATAATCTT ATTTATACCT CAGTTTGCAT 1620
ATTTTTTTAC TATTTAGAAT GTAGCCCTTT TTGTACTGAT ATAATTTAGT TCCACAAATG 1680
GTGGGTACAA AAAGTCAAGT TTGTGGCTTA TGGATTCATA TAGGCCAGAG TTGCAAAGAT 1740
CTTTTCCAGA GTATGCAACT CTGACGTTGA TCCCAGAGAG CAGCTTCAGT GACAAACATA 1800
TCCTTTCAAG ACAGAAAGAG ACAGGAGACA TGAGTCTTTG CCGGAGGAAA AGCAGCTCAA 1860
GAACACATGT GCAGTCACTG GTGTCACCCT GGATAGGCAA GGGATAACTC TTCTAACACA 1920
AAATAAGTGT TTTATGTTTG GAATAAAGTC AACCTTGTTT CTACTGTTTT

AAC3 DNA sequence
Gene name: Branched chain aminotransferase 1, cytosolic
Unigene number: Hs.157205
Probeset Accession #: AA423987
Nucleic Acid Accession #: NM_005504 cluster
Coding sequence: 1-1155 (predicted start/stop codons underlined)

ATGGATTGCA GTAACGGATC GGCAGAGTGT ACCGGAGAAG GAGGATCAAA AGAGGTGGTG 60
GGGACTTTTA AGGCTAAAGA CCTAATAGTC ACACCAGCTA CCATTTTAAA GGAAAAACCA 120
GACCCCAATA ATCTGGTTTT TGGAACTGTG TTCACGGATC ATATGCTGAC GGTGGAGTGG 180
TCCTCAGAGT TTGGATGGGA GAAACCTCAT ATCAAGCCTC TTCAGAACCT GTCATTGCAC 240
CCTGGCTCAT CAGCTTTGCA CTATGCAGTG GAATTATTTG AAGGATTGAA GGCATTTCGA 300
GGAGTAGATA ATAAAATTCG ACTGTTTCAG CCAAACCTCA ACATGGATAG AATGTATCGC 360

TCTGCTGTGA GGGCAACTCT GCCGGTATTT GACAAAGAAG AGCTCTTAGA GTGTATTCAA 420
CAGCTTGTGA AATTGGATCA AGAATGGGTC CCATATTCAA CATCTGCTAG TCTGTATATT 480
CGTCCTGCAT TCATTGGAAC TGAGCCTTCT CTTGGAGTCA AGAAGCCTAC CAAAGCCCTG 540
CTCTTTGTAC TCTTGAGCCC AGTGGGACCT TATTTTTCAA GTGGAACCTT TAATCCAGTG 600
TCCCTGTGGG CCAATCCCAA GTATGTAAGA GCCTGGAAAG GTGGAACTGG GGACTGCAAG 660
ATGGGAGGGA ATTACGGCTC ATCTCTTTTT GCCCAATGTG AAGACGTAGA TAATGGGTGT 720
CAGCAGGTCC TGTGGCTCTA TGGCAGAGAC CATCAGATCA CTGAAGTGGG AACTATGAAT 780
CTTTTTCTTT ACTGGATAAA TGAAGATGGA GAAGAAGAAC TGGCAACTCC TCCACTAGAT 840
GGCATCATTC TTCCAGGAGT GACAAGGCGG TGCATTCTGG ACCTGGCACA TCAGTGGGGT 900
GAATTTAAGG TGTCAGAGAG ATACCTCACC ATGGATGACT TGACAACAGC CCTGGAGGGG 960
AACAGAGTGA GAGAGATGTT TAGCTCTGGT ACAGCCTGTG TTGTTTGCCC AGTTTCTGAT 1020
ATACTGTACA AAGGCGAGAC AATACACATT CCAACTATGG AGAATGGTCC TAAGCTGGCA 1080
AGCCGCATCT TGAGCAAATT AACTGATATC CAGTATGGAA GAGAAGAGAG CGACTGGACA 1140
ATTGTGCTAT CCTGA 1155

ACG4 DNA sequence:
Gene name: Pentaxin-related gene, rapidly induced by IL-1 beta
Unigene number: Hs.2050
Probeset Accession #: M31166
Nucleic Acid Accession #: NM_002852 cluster
Coding sequence: 68-1213 (predicted start/stop codons underlined)

CTCAAACTCA GCTCACTTGA GAGTCTCCTC CCGCCAGCTG TGGAAAGAAC TTTGCGTCTC 60
TCCAGCAATG CATCTCCTTG CGATTCTGTT TTGTGCTCTC TGGTCTGCAG TGTTGGCCGA 120
GAACTCGGAT GATTATGATC TCATGTATGT GAATTTGGAC AACGAAATAG ACAATGGACT 180
CCATCCCACT GAGGACCCCA CGCCGTGCGA CTGCGGTCAG GAGCACTCGG AATGGGACAA 240
GCTCTTCATC ATGCTGGAGA ACTCGCAGAT GAGAGAGCGC ATGCTGCTGC AAGCCACGGA 300
CGACGTCCTG CGGGGCGAGC TGCAGAGGCT GCGGGAGGAG CTGGGCCGGC TCGCGGAAAG 360
CCTGGCGAGG CCGTGCGCGC CGGGGGCTCC CGCAGAGGCC AGGCTGACCA GTGCTCTGGA 420
CGAGCTGCTG CAGGCGACCC GCGACGCGGG CCGCAGGCTG GCGCGTATGG AGGGCGCGGA 480
GGCGCAGCGC CCAGAGGAGG CGGGGCGCGC CCTGGCCGCG GTGCTAGAGG AGCTGCGGCA 540
GACGCGAGCC GACCTGCACG CGGTGCAGGG CTGGGCTGCC CGGAGCTGGC TGCCGGCAGG 600
TTGTGAAACA GCTATTTTAT TCCCAATGCG TTCCAAGAAG ATTTTTGGAA GCGTGCATCC 660
AGTGAGACCA ATGAGGCTTG AGTCTTTTAG TGCCTGCATT TGGGTCAAAG CCACAGATGT 720
ATTAAACAAA ACCATCCTGT TTTCCTATGG CACAAAGAGG AATCCATATG AAATCCAGCT 780
GTATCTCAGC TACCAATCCA TAGTGTTTGT GGTGGGTGGA GAGGAGAACA AACTGGTTGC 840
TGAAGCCATG GTTTCCCTGG GAAGGTGGAC CCACCTGTGC GGCACCTGGA ATTCAGAGGA 900
AGGGCTCACA TCCTTGTGGG TAAATGGTGA ACTGGCGGCT ACCACTGTTG AGATGGCCAC 960
AGGTCACATT GTTCCTGAGG GAGGAATCCT GCAGATTGGC CAAGAAAAGA ATGGCTGCTG 1020
TGTGGGTGGT GGCTTTGATG AAACATTAGC CTTCTCTGGG AGACTCACAG GCTTCAATAT 1080
CTGGGATAGT GTTCTTAGCA ATGAAGAGAT AAGAGAGACC GGAGGAGCAG AGTCTTGTCA 1140
CATCCGGGGG AATATTGTTG GGTGGGGAGT CACAGAGATC CAGCCACATG GAGGAGCTCA 1200
GTATGTTTCA TAAATGTTGT GAAACTCCAC TTGAAGCCAA AGAAAGAAAC TCACACTTAA 1260
AACACATGCC AGTTGGGAAG GTCTGAAAAC TCAGTGCATA ATAGGAACAC TTGAGACTAA 1320
TGAAAGAGAG AGTTGAGACC AATCTTTATT TGTACTGGCC AAATACTGAA TAAACAGTTG 1380
AAGGAAAGAC ATTGGAAAAA GCTTTTGAGG ATAATGTTAC TAGACTTTAT GCCATGGTGC 1440
TTTCAGTTTA ATGCTGTGTC TCTGTCAGAT AAACTCTCAA ATAATTAAAA AGGACTGTAT 1500
TGTTGAACAG AGGGACAATT GTTTTACTTT TCTTTGGTTA ATTTTGTTTT GGCCAGAGAT 1560
GAATTTTACA TTGGAAGAAT AACAAAAATAA GATTTGTTGT CCATTGTTCA TTGTTATTGG 1620
TATGTACCTT ATTACAAAAA AAATGATGAA AACATATTTA TACTACAAGG TGACTTAACA 1680
ACTATAAATG TAGTTTATGT GTTATAATCG AATGTCACGT TTTTGAGAAG ATAGTCATAT 1740
AAGTTATATT GCAAAAGGGA TTTGTATTAA TTTAAGACTA TTTTTGTAAA GCTCTACTGT 1800
AAATAAAATA TTTTATAAAA CTAAAAAAAA AAAAAAA 1837

ACR5 DNA sequence
Gene name: Von Willebrand factor, coagulation factor VIII
Unigene number: Hs.110802
Probeset Accession #: M10321
Nucleic Acid Accession #: NM_000552
Coding sequence: 311-8752 (predicted start/stop codons underlined)

AGCTCACAGC TATTGTGGTG GGAAAGGGAG GGTGGTTGGT GGATGTCACA GCTTGGGCTT 60
TATCTCCCCC AGCAGTGGGG ACTCCACAGC CCCTGGGCTA CATAACAGCA AGACAGTCCG 120
GAGCTGTAGC AGACCTGATT GAGCCTTTGC AGCAGCTGAG AGCATGGCCT AGGGTGGGCG 180
GCACCATTGT CCAGCAGCTG AGTTTCCCAG GGACCTTGGA GATAGCCGCA GCCCTCATTT 240
GCAGGGGAAG GCACCATTGT CCAGCAGCTG AGTTTCCCAG GGACCTTGGA GATAGCCGCA 300

GCCCTCATTT ATGATTCCTG CCAGATTTGC CGGGGTGCTG CTTGCTCTGG CCCTCATTTT 360
GCCAGGGACC CTTTGTGCAG AAGGAACTCG CGGCAGGTCA TCCACGGCCC GATGCAGCCT 420
TTTCGGAAGT GACTTCGTCA ACACCTTTGA TGGGAGCATG TACAGCTTTG CGGGATACTG 480
CAGTTACCTC CTGGCAGGGG GCTGCCAGAA ACGCTCCTTC TCGATTATTG GGGACTTCCA 540
GAATGGCAAG AGAGTGAGCC TCTCCGTGTA TCTTGGGGAA TTTTTTGACA TCCATTTGTT 600
TGTCAATGGT ACCGTGACAC AGGGGGACCA AAGAGTCTCC ATGCCCTATG CCTCCAAAGG 660
GCTGTATCTA GAAACTGAGG CTGGGTACTA CAAGCTGTCC GGTGAGGCCT ATGGCTTTGT 720
GGCCAGGATC GATGGCAGCG GCAACTTTCA AGTCCTGCTG TCAGACAGAT ACTTCAACAA 780
GACCTGCGGG CTGTGTGGCA ACTTTAACAT CTTTGCTGAA GATGACTTTA TGACCCAAGA 840
AGGGACCTTG ACCTCGGACC CTTATGACTT TGCCAACTCA TGGGCTCTGA GCAGTGGAGA 900
ACAGTGGTGT GAACGGGCAT CTCCTCCCAG CAGCTCATGC AACATCTCCT CTGGGGAAAT 960
GCAGAAGGGC CTGTGGGAGC AGTGCCAGCT TCTGAAGAGC ACCTCGGTGT TTGCCCGCTG 1020
CCACCCTCTG GTGGACCCCG AGCCTTTTGT GGCCCTGTGT GAGAAGACTT TGTGTGAGTG 1080
TGCTGGGGGG CTGGAGTGCG CCTGCCCTGC CCTCCTGGAG TACGCCCGGA CCTGTGCCCA 1140
GGAGGGAATG GTGCTGTACG GCTGGACCGA CCACAGCGCG TGCAGCCCAG TGTGCCCTGC 1200
TGGTATGGAG TATAGGCAGT GTGTGTCCCC TTGCGCCAGG ACCTGCCAGA GCCTGCACAT 1260
CAATGAAATG TGTCAGGAGC GATGCGTGGA TGGCTGCAGC TGCCCTGAGG GACAGCTCCT 1320
GGATGAAGGC CTCTGCGTGG AGAGCACCGA GTGTCCCTGC GTGCATTCCG GAAAGCGCTA 1380
CCCTCCCGGC ACCTCCCTCT CTCGAGACTG CAACACCTGC ATTTGCCGAA ACAGCCAGTG 1440
GATCTGCAGC AATGAAGAAT GTCCAGGGGA GTGCCTTGTC ACTGGTCAAT CCCACTTCAA 1500
GAGCTTTGAC AACAGATACT TCACCTTCAG TGGGATCTGC CAGTACCTGC TGGCCCGGGA 1560
TTGCCAGGAC CACTCCTTCT CCATTGTCAT TGAGACTGTC CAGTGTGCTG ATGACCGCGA 1620
CGCTGTGTGC ACCCGCTCCG TCACCGTCCG GCTGCCTGGC CTGCACAACA GCCTTGTGAA 1680
ACTGAAGCAT GGGGCAGGAG TTGCCATGGA TGGCCAGGAC ATCCAGCTCC CCCTCCTGAA 1740
AGGTGACCTC CGCATCCAGC ATACAGTGAC GGCCTCCGTG CGCCTCAGCT ACGGGGAGGA 1800
CCTGCAGATG GACTGGGATG GCCGCGGGAG GCTGCTGGTG AAGCTGTCCC CCGTCTACGC 1860
CGGGAAGACC TGCGGCCTGT GTGGGAATTA CAATGGCAAC CAGGGCGACG ACTTCCTTAC 1920
CCCCTCTGGG CTGGCAGAGC CCCGGGTGGA GGACTTCGGG AACGCCTGGA AGCTGCACGG 1980
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AAC7 DNA sequence
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Nucleic Acid Accession #: AB037715
Coding sequence: 370-3489 (predicted start/stop codons underlined)

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ACG8 DNA sequence
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Unigene number: Hs.21806 (3'UTR only)
Probeset Accession #: AA398243

Nucleic Acid Accession #: AF301463 cluster
Coding sequence: 9-2255 (predicted start/stop codons underlined)

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ACN1 DNA sequence
Gene name: EST
Unigene number: Hs.30089
Probeset Accession #: AA410480
CAT cluster#: 96816_1
Coding sequence: Partial sequence, possible frameshift. Predicted stop codon underlined.

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ACJ2 DNA sequence
Gene name: Complement component C1q receptor
Unigene number: Hs.97199
Probeset Accession #: AA487558
Nucleic Acid Accession #: NM_012072
Coding sequence: 149-2107. Predicted start/stop codons underlined

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ACJ3 DNA sequence
Gene name: FLT1/vascular endothelial growth factor receptor
Unigene number: Hs.138671
Probeset Accession #: AA047437
Nucleic Acid Accession #: NM_002019
Coding sequence: 250-4266 (predicted start/stop codons underlined)

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GCAAATTTTA GACCTTTACC TATGGAAGTG GTTCTATGTC CATTCTCATT CGTGGCATGT 5040
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TAAGATGCAC TGAAAACTTA GCCAGAGTTA GGTTGTCTCC AGGCCATGAT GGCCTTACAC 5160
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TTGGTATTAT TCTGTTTTGC ACAGTTAGTT GTGAAAGAAA GCTGAGAAGA ATGAAAATGC 5280
AGTCCTGAGG AGAGTTTTCT CCATATCAAA ACGAGGGCTG ATGGAGGAAA AAGGTCAATA 5340
AGGTCAAGGG AAGACCCCGT CTCTATACCA ACCAAACCAA TTCACCAACA CAGTTGGGAC 5400
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ACTAATCTGA AAGGATGTGG AAGAGCATTA GCTGGCGCAT ATTAAGCACT TTAAGCTCCT 5520
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ACJ9 DNA sequence
Gene name: Purine nucleoside phosphorylase
Unigene number: Hs.75514
Probeset Accession #: K02574
Nucleic acid Accession #: X00737 cluster
Coding sequence: 110-979 (predicted start/stop codons underlined)

AACTGTGCGA ACCAGACCCG GCAGCCTTGC TCAGTTCAGC ATAGCGGAGC GGATCCGATC 60
GGATCGGAGC ACACCGGAGC AGGCTCATCG AGAAGGCGTC TGCGAGACCA TGGAGAACGG 120
ATACACCTAT GAAGATTATA AGAACACTGC AGAATGGCTT CTGTCTCATA CTAAGCACCG 180
ACCTCAAGTT GCAATAATCT GTGGTTCTGG ATTAGGAGGT CTGACTGATA AATTAACTCA 240
GGCCCAGATC TTTGACTACA GTGAAATCCC CAACTTTCCT CGAAGTACAG TGCCAGGTCA 300
TGCTGGCCGA CTGGTGTTTG GGTTCCTGAA TGGCAGGGCC TGTGTGATGA TGCAGGGCAG 360

GTTCCACATG TATGAAGGGT ACCCACTCTG GAAGGTGACA TTCCCAGTGA GGGTTTTCCA 420
CCTTCTGGGT GTGGACACCC TGGTAGTCAC CAATGCAGCA GGAGGGCTGA ACCCCAAGTT 480
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GAACCCTCTC AGAGGGCCCA ATGATGAAAG GTTTGGAGAT CGTTTCCCTG CCATGTCTGA 600
TGCCTACGAC CGGACTATGA GGCAGAGGGC TCTCAGTACC TGGAAACAAA TGGGGGAGCA 660
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GTAGCTGCTA CCTTCTTTGG CCCCTTGCTG GAGTCATGTG CCTCTGTCCT TAGGTTGTAG 1080
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TGCCAGATCC TCTTCTCAAA GCTGGGATTA CAGGTGTGAG CATAGTGAGA CCTTGGCGCT 1200
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ACCACACATC TGTGGAGATG CCCAGGATTT GACTCGGGCC TTAGAACTTT GCATAGCAGC 1320
TGCTACTAGC TCTTTGAGAT AATACATTCC GAGGGGCTCA GTTCTGCCTT ATCTAAATCA 1380
CCAGAGACCA AACAAGGACT AATCCAATAC CTCTTGGA

ACK4 DNA sequence
Gene name: EST
Unigene number: Hs.265499
Probeset Accession #: R68763
CAT cluster#: Cluster 46668_2
Sequence: Both the EST corresponding to the probeset accession and exon prediction; number and the CAT cluster align with the Homo sapiens BAC clone AC009414 RP11-490M8. Using FGENESH, 2 exons predicted on this BAC clone upstream of the probeset.
Predicted exon 1: bases 5808-5887 of BAC clone AC009414

AAAGTCTCGC CCAAACTTTG TTCGGCACAA CCAGCGCCGA GGGGGCGGCG CAGGCCAGGT 60
GGGAGGGGGC CCGCAGCGGG CGGCCGTACC TTCGCAAACG CCCGCTTCGT ACTCGGTGAG 120
GGAGTCGCCA TTGAGCGGGG GGCGGATGAC ACAACGCAGC CCCCGGTCGC AGGTTCCGTA 180
AATCCCGAAG GTGCCGCCGC AGCTCTCGTT CCTCTGGCTG GCGCACGTGT AGCAGCAGCC 240
GCAGACGCCC TGCACGATGC TCCCCGGGCA GTTCCTGGGC TCCTCGCACT TGGACTCGTC 300
ACAGGGCAGG CAGACCAGCG CCCGGGTGCC GGAGCGCGCC AGCAGCAGCA GCAGCCCCAG 360
CAGCGAGACC AGGAGGTGCC CGCAGCCGGC CAACCCCCTG TCCCCCGCCA CCAAGTACAT 420
CCTCCTGCGC CGCCGCCGCC TCCTCCTCGC AGCCGGGCCG GGAGCGGGGC GGGCGCCCTC 480
CCCTGCGCGG GGCACACGCG CCGCCGCCGC CGCACCAGCA GCCCGCGGTC CTCACCGCCC 540
CTCTCGGGGC CCCCGGGGCG CGCCTCCCCT CGCGGGGCGA GGCCCCCGCC CCTTCTGCGG 600
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TCAACCCAAA CTTCTGGCGC GGCGGCGGCG GTGGCTGCTG CGCTCGGCTC CAGCCCGGGC 780
CGGCGGCGCC TCCTCCCTCT CCTCCTCCGA GTCGGCCGGC CCCGCAGCGG CGCAGCCTCC 840
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CTTCCCCCCA CCCCCACGCG CCGCGCGCCG CTCATTGGCT GCCCCCCCTC CCCGGCCCGG 1080
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CACGCCTCCA CCTCTTCCCG ATCTCCTCCT CCCCGAGCCC GGCGCACCGA GCCGGCCGTG 1200
CCACCGAGCT GCGGCTCTGG CCCCGGCGCC GCGGGTGCGC TGCGGATGGG CTTGGGGCGC 1260
ACCCAGCGAG CAGCGAGAGT CGCGGTGTCC CGGGCGCTCG CTGGCACCGT GGCCGCAGCG 1320
GCCGGCCTGG GAGCCAGGAG GGCGAGGCGG CTGCACCTTC GGGGCCAGAT TGGAGTTCGA 1380
AGAGTGGCGG GTACCCCAGA AGCTCGGGGC CGGGGCGATG GCTGCAGCCT CGGGAGGGTA 1440
TCGCCGGATC GAACTCCGGG AAAGGGAAGC AAAGGCATGG AACCTCCGCA CACTGGATGA

Predicted ACK4 gene seq (predicted start/stop codons underlined)

ATGCCCCCGG AACAGCATCA TCAGCCCAAC AAAGTCTCGC CCAAACTTTG TTCGGCACAA 60
CCAGCGCCGA GGGGGCGGCG CAGGCCAGGT GGGAGGGGGC CCGCAGCGGG CGGCCGTACC 120
TTCGCAAACG CCCGCTTCGT ACTCGGTGAG GGAGTCGCCA TTGAGCGGGG GGCGGATGAC 180
ACAACGCAGC CCCCGGTCGC AGGTTCCGTA AATCCCGAAG GTGCCGCCGC AGCTCTCGTT 240
CCTCTGGCTG GCGCACGTGT AGCAGCAGCC GCAGACGCCC TGCACGATGC TCCCCGGGCA 300
GTTCCTGGGC TCCTCGCACT TGGACTCGTC ACAGGGCAGG CAGACCAGCG CCCGGGTGCC 360
GGAGCGCGCC AGCAGCAGCA GCAGCCCCAG CAGCGAGACC AGGAGGTGCC CGCAGCCGGC 420
CAACCCCCTG TCCCCCGCCA CCAAGTACAT CCTCCTGCGC CGCCGCCGCC TCCTCCTCGC 480
AGCCGGGCCG GGAGCGGGGC GGGCGCCCTC CCCTGCGCGG GGCACACGCG CCGCCGCCGC 540

CGCACCAGCA GCCCGCGGTC CTCACCGCCC CTCTCGGGGC CCCCGGGGCG CGCCTCCCCT 600
CGCGGGGCGA GGCCCCCGCC CCTTCTGCGG GCCGCGCCGA CCCCGAGCCC ACGAGCCTTG 660
GCGCCGGCGG CAGCTTCCCC TCCTCCTCCT CCTCCTCCTC CCGGGAGGGA GGGGGAAAAA 720
AGAAAAAAGT TTCCTCCCGG CAGCTCCGGT TCAACCCAAA CTTCTGGCGC GGCGGCGGCG 780
GTGGCTGCTG CGCTCGGCTC CAGCCCGGGC CGGCGGCGCC TCCTCCCTCT CCTCCTCCGA 840
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CCCTCCCCCA TCCTACCTCC TCCCCCAGAC CTTCCCCCCA CCCCCACGCG CCGCGCGCCG 1080
CTCATTGGCT GCCCCCCCTC CCCGGCCCGG CCGGCCCCCT CCGCCTCCCC CTCCCCCTCT 1140
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AAAGGCATGG AACCTCCGCA CACTGGATGA

AAA8 DNA sequence
Gene name: ETL protein, with extended open reading frame
Unigene number: Hs.57958
Probeset Accession #: D58024
Nucleotide Accession #: AF192403
Coding sequence: 151-2136. Underlined sequences correspond to extended sequence not included in AF192403.

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ATCACTAATG ATGGAACCGT CTGTATAGAA AATGTGAATG CAAACTGCCA TTTAGATAAT 420
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ATTACATATA TAGAAATATT AGCTGAATCA TCTTCATTAC TAGGTTACAA GAACAACACT 600
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TTATTTCACA GATTGTGACT TTGGATAGTT AATCAGTAAA ATATAAATGT GTCGA

AAC6 DNA sequence
Gene name: Homo sapiens cDNA FLJ13465 fis, clone PLACE1003493, weakly similar to endothelial cell multimerin precursor
Unigene number: Hs.234797
Probeset Accession #: AA025351
Nucleotide Accession #: AK023527
Coding sequence: predicted 75-2921
Extended sequence: 729-3465 (underlined sequence)

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TGAAGATGCC TTGGTTCCTC TTCACTGTCT GCCATGATTG TAAGTTTCCT GAGGCCTCCC 3780
CAGCCATGTG GAACAGTGAG TCAATTAAAC CTCTTTCCTT TATAAATT

ACH7 DNA sequence
Gene name: ESTs
Unigene number: Hs.3807
Probeset Accession #: AA292694
BAC Accession #: AL161751
FGENESH predicted exons: FGENESH predicts 2 exons on the minus strand of AL161751 upstream of the ACH7 probeset.

FGENESH predicted exon 1:
ATGGGCAAAG ACTTCATGAC TAAAACACCA AAAGCATTTG CAACAAAAGC CAAAATTGAC 60
AAATGGGATC TAATTAAACT AAAGAGCTTC TGCACAGCAA AAGAAACTAT CATCAGAGTG 120
AACAGTCAAC CTACAGACTG GCAGAAAACT TTTGCAATCT ATCCATCTGA CAAAGGGGTA 180
ATAGCCAGAA TCTACAAGGA GCTTGAACAA ATTTATAAGA AAAAAAAACC AACAAAAA

FGENESH predicted exon 2:
CGCTCCGCAC ACATTTCCTG TCGCGGCCTA AGGGAAACTG TTGGCCGCTG GGCCCGCGGG 60
GGGATTCTTG GCAGTTGGGG GGTCCGTCGG GAGCGAGGGC GGAGGGGAAG GGAGGGGGAA 120
CCGGGTTGGG GAAGCCAGCT GTAGAGGGCG GTGACCGCGC TCCAGACACA GCTCTGCGTC 180
CTCGAGCGGG ACAGATCCAA GTTGGGAGCA GCTCTGCGTG CGGGGCCTCA GAGAATGAGG 240
CCGGCGTTCG CCCTGTGCCT CCTCTGGCAG GCGCTCTGGC CCGGGCCGGG CGGCGGCGAA 300
CACCCCACTG CCGACCGTGC TGGCTGCTCG GCCTCGGGGG CCTGCTACAG CCTGCACCAC 360
GCTACCATGA AGCGGCAGGC GGCCGAGGAG GCCTGCATCC TGCGAGGTGG GGCGCTCAGC 420
ACCGTGCGTG CGGGCGCCGA GCTGCGCGCT GTGCTCGCGC TCCTGCGGGC AGGCCCAGGG 480
CCCGGAGGGG GCTCCAAAGA CCTGCTGTTC TGGGTCGCAC TGGAGCGCAG GCGTTCCCAC 540
TGCACCCTGG AGAACGAGCC TTTGCGGGGT TTCTCCTGGC TGTCCTCCGA CCCCGGCGGT 600
CTCGAAAGCG ACACGCTGCA GTGGGTGGAG GAGCCCCAAC GCTCCTGCAC CGCGCGGAGA 660
TGCGCGGTAC TCCAGGCCAC CGGTGGGGTC GAGCCCGCAG CTGGAAGGAG ATGCGATGCC 720
ACCTGCGCGC CAACGGCTAC CTGTGCAAGT ACCAGTTTGA GGTCTTGTGT CCTGCGCCGC 780
GCCCCGGGGC CGCCTCTAAC TTGAGCTATC GCGCGCCCTT CCAGCTGCAC AGCGCCGCTC 840
TGGACTTCAG TCCACCTGGG ACCGAGGTGA GTGCGCTCTG CCGGGGACAG CTCCCGATCT 900
CAGTTACTTG CATCGCGGAC GAAATCGGCG CTCGCTGGGA CAAACTCTCG GGCGATGTGT 960
TGTGTCCCTG CCCCGGGAGG TACCTCCGTG CTGGCAAATG CGCAGAGCTC CCTAACTGCC 1020
TAGACGACTT GGGAGGCTTT GCCTGCGAAT GTGCTACGGG CTTCGAGCTG GGGAAGGACG 1080
GCCGCTCTTG TGTGACCAGT GGGGAAGGAC AGCCGACCCT TGGGGGGACC GGGGTGCCCA 1140
CCAGGCGCCC GCCGGCCACT GCAACCAGCC CCGTGCCGCA GAGAACATGG CCAATCAGGG 1200
TCGACGAGAA GCTGGGAGAG ACACCACTTG TCCCTGAACA AGACAATTCA GTAACATCTA 1260
TTCCTGAGAT TCCTCGATGG GGATCACAGA GCACGATGTC TACCCTTCAA ATGTCCCTTC 1320
AAGCCGAGTC AAAGGCCACT ATCACCCCAT CAGGGAGCGT GATTTCCAAG TTTAATTCTA 1380
CGACTTCCTC TGCCACTCCT CAGGCTTTCG ACTCCTCCTC TGCCGTGGTC TTCATATTTG 1440
TGAGCACAGC AGTAGTAGTG TTGGTGATCT TGACCATGAC AGTACTGGGG CTTGTCAAGC 1500
TCTGCTTTCA CGAAAGCCCC TCTTCCCAGC CAAGGAAGGA GTCTATGGGC CCGCCGGGCC 1560
TGGAGAGTGA TCCTGAGCCC GCTGCTTTGG GCTCCAGTTC TGCACATTGC ACAAACAATG 1620
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CCCCTCTTGG CTCTAGTGAT GCATAG

ACH7 predicted coding seq (predicted start/stop codons underlined)
ATGGGCAAAG ACTTCATGAC TAAAACACCA AAAGCATTTG CAACAAAAGC CAAAATTGAC 60
AAATGGGATC TAATTAAACT AAAGAGCTTC TGCACAGCAA AAGAAACTAT CATCAGAGTG 120
AACAGTCAAC CTACAGACTG GCAGAAAACT TTTGCAATCT ATCCATCTGA CAAAGGGGTA 180
ATAGCCAGAA TCTACAAGGA GCTTGAACAA ATTTATAAGA AAAAAAAACC AACAAAAACG 240
CTCCGCACAC ATTTCCTGTC GCGGCCTAAG GGAAACTGTT GGCCGCTGGG CCCGCGGGGG 300

GATTCTTGGC AGTTGGGGGG TCCGTCGGGA GCGAGGGCGG AGGGGAAGGG AGGGGGAACC 360
GGGTTGGGGA AGCCAGCTGT AGAGGGCGGT GACCGCGCTC CAGACACAGC TCTGCGTCCT 420
CGAGCGGGAC AGATCCAAGT TGGGAGCAGC TCTGCGTGCG GGGCCTCAGA GAATGAGGCC 480
GGCGTTCGCC CTGTGCCTCC TCTGGCAGGC GCTCTGGCCC GGGCCGGGCG GCGGCGAACA 540
CCCCACTGCC GACCGTGCTG GCTGCTCGGC CTCGGGGGCC TGCTACAGCC TGCACCACGC 600
TACCATGAAG CGGCAGGCGG CCGAGGAGGC CTGCATCCTG CGAGGTGGGG CGCTCAGCAC 660
CGTGCGTGCG GGCGCCGAGC TGCGCGCTGT GCTCGCGCTC CTGCGGGCAG GCCCAGGGCC 720
CGGAGGGGGC TCCAAAGACC TGCTGTTCTG GGTCGCACTG GAGCGCAGGC GTTCCCACTG 780
CACCCTGGAG AACGAGCCTT TGCGGGGTTT CTCCTGGCTG TCCTCCGACC CCGGCGGTCT 840
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TGCTTTCACG AAAGCCCCTC TTCCCAGCCA AGGAAGGAGT CTATGGGCCC GCCGGGCCTG 1800
GAGAGTGATC CTGAGCCCGC TGCTTTGGGC TCCAGTTCTG CACATTGCAC AAACAATGGG 1860
GTGAAAGTCG GGGACTGTGA TCTGCGGGAC AGAGCAGAGG GTGCCTTGCT GGCGGAGTCC 1920
CCTCTTGGCT CTAGTGATGC ATAG

AAD3 DNA sequence
Gene name: ESTs
Unigene number: Hs.17404
Probeset Accession #: N39584
Nucleic Acid Accession #: N39584
Coding sequence: no identified ORF; possible frameshifts

AAATGGGATT GAGTTAAAAC TATTTTATTT TAAATATACA TTTTAAAGCA GTTCTTTTTT 60
TTTTTTTTTT TTTTATTATA CACACACTTC AAGAGAATAT GCACAGTCTA GGCCGGGCAC 120
GGTGGCTCAC GCCTGTAATC CCAGCACTTT GGGAGGCCGA GGCATGTGGA TCACCTGAGG 180
TCAGGAGTTT GAGACCAGCC TAGACAACAT GGTGAAACCT TGTCTCTATG AAAAATACAA 240
AATTTGCTGG GAGTGGTGGT GCATGCCTGT AATCCCAGCT ACTTGGAAGG CTGAGGCAGG 300
AGAATGTCTT GAACCTAGGA GGTGGAGGTT GCAGTGAGCT GAGATTGCAC CATTGCACTC 360
CAGCCTGTGC AACAAAAGTG AAACTCCATT TCAAGAAAAA AAAAAAAAAA AGAATATGCA 420
CAGTCTGAAT GTATACCAGG AGTGTGAGAG ACACATGCCC ACTTCATGCA ACTCCTAAAC 480
TCAAAGTCTA AATCAGATAT TTTTATTAAC AATGACAACT TGTTGCCAAC TCCCTGTTTC 540
TAATCACCAA AGACCCAGGG TACCTAAAAG GACTTTGCAA CCAAGCAAAG TCACTGTCTT 600
CAAATCTGGA TACACACTTT CCCCTCTGTA GATTCAAAAG GTGCTTCCTT CCCGGCTGTC 660
TCCAGCTTCC TTACTCTCTT TTCTGGGATT TCTTTTTCTT CTTTCTTTCT GGCTCTTCCT 720
CCACTGGCTG AACTGGGTCC CCTAACTGAA ACAGCCCCTG ACTTAGCCCA AGCATGCTTC 780
CTTTAGCTGC TGTGAGAATT TTGTCTTCCT CACCAGCCAG GTCCTCAAGG CAAAGTCCTC 840
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TTTCCTGTAT GAAATATGTT TTATATAATC TCCTATTATT TTTATCTTAT GTTTTGTATT 1080
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AAAAAAAAAA AAAAAAAAAA AAAAAAAA

AAD4 DNA sequence
Gene name: ERG
Unigene number: Hs.279477 / Hs.45514
Probeset Accession #: R32894
Nucleic Acid Accession #: M17254

Coding sequence: 257-1645 (predicted start/stop codons underlined)

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AAAGATGGCA GAACCAAGGG CAACTAAAGC CGTCAGGTTC TGAACAGCTG GTAGATGGGC    240
TGGCTTACTG AAGGACATGA TTCAGACTGT CCCGGACCCA GCAGCTCATA TCAAGGAAGC    300
CTTATCAGTT GTGAGTGAGG ACCAGTCGTT GTTTGAGTGT GCCTACGGAA CGCCACACCT    360
GGCTAAGACA GAGATGACCG CGTCCTCCTC CAGCGACTAT GGACAGACTT CCAAGATGAG    420
CCCACGCGTC CCTCAGCAGG ATTGGCTGTC TCAACCCCCA GCCAGGGTCA CCATCAAAAT    480
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TACAATATGA AGTTATTAGT TCTTAGAATG CAGAATGTAT GTAATAAAAT AAGCTTGGCC   3000
TAGCATGGCA AATCAGATTT ATACAGGAGT CTGCATTTGC ACTTTTTTTA GTGACTAAAG   3060
TTGCTTAATG AAAACATGTG CTGAATGTTG TGGATTTTGT GTTATAATTT ACTTTGTCCA   3120
GGAACTTGTG CAAGGGAGAG CCAAGGAAAT AGGATGTTTG GCACCC
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AADS DNA sequence
Gene name: activin A receptor type II-like 1 (ALK-1)
Unigene number: Hs.8881 / Hs.172670
Probeset Accession #: T57112
Nucleic Acid Accession #: NM_000020
Coding sequence: 283-1794 (predicted start/stop codons underlined)

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AAD8 DNA sequence
Gene name: ESTs
Unigene number: Hs.144953
Probeset Accession #: AA404418
Nucleic Acid Accession #: n/a
Coding sequence: no ORF identified; possible frameshifts

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TGCTTGACCT AAAGACAGAC AATTCTTTCC CCAAACTTTG CTGTTTCTTT TTTGAGTCTT    240
TGTTGAAAGA TTTCTTTTAA AAGGCGTTCG TGTGAGAAGA TCACAGCAAC AAATCTGGCT    300
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TATTGAAAGG CCATATTGAG GCTCCATTGA TTTTTTTTCC TGCATATTTA TCAGTATCGA   1140
ATTAGAAAAT TGAACCTTCA GTGTTACTAG ATGGAAATCT ACCAAAAAGT AGCAAGGTTT   1200
ACGAATGGTG GGATTTATTG GTGATTAAAC ATTTTTTTCC TGTATTTTAT AAGTTTCACA   1260
TTACATTTAC AATGAGAAAA AAATGTAAAT GTAGAATTAA AGTCTTGTTA ATATCGTAAT   1320
TTGCCTATTG CTGTACTAAA AGAAGCTTCT ATAAAATGTA TCATTCTCAT CCTTAGATTC   1380
AGGCCAGAAA GTAACTTTCA GTGTTAGGTA TTTGAAATAA TGCAGCCTGT CATATGTACT   1440
CTGGTTACCA GAATGAAAAA ACAAAAAGAG ATACATACAT AGTAAGGAAA CATGAAATTG   1500
GAGGAATTGA TCCCCATGTG TATTGCAGCT TCATATACCA GTAGTCTCTA ATAAGTCATT   1560
GCTTTAATAA AAAAAAAAAT AGAAAATTTA AA
```

ACA2 DNA sequence
Gene name: EST
Unigene number: Hs.16450
Probeset Accession #: AA478778
Nucleic Acid Accession #: AA478778
Coding sequence: no ORF identified; possible frameshifts

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TATTTTTGTA CGTAAAATGA TTCTATTATG ACTGCCTTTG CATGTAGTAA TATGACAAAG     60
TGATCCTTCA TTATCACGGT ACACTATTGT TTACTTTTCA TCTGTAAATG TTTTATTGTT    120
ACTTTTTTAA AATGAATTTT TTTAAAACAA TCTAGCCATC ATCAAGGTGC TATAAGAGTT    180
GTATAAAAGA TATTTTTGGC ATTTCTAGGC AAGTATCAGC CAATAAGTAT GTTAGTGATA    240
TCACAGATTG TACCAACTAT TAACTATGTT AAATAAGTAT TCAGTTTCAT GTGATCTCTG    300
GGAAAAAAAT ATGCTGCCTT GGTGCTAATA TTGTATGTAT TTAAATGATC ATCTGACTCA    360
GAAATATAAA CACTTTTAAT GAAAGGGAGG AACGGAAGGA CAATTTCCAG TGCACAGAAT    420
CACTTGGATG AAATAAGACC AGCTCTTTAC CCTTATTTTT GGATATGCCT TTTTTGGAAG    480
AGACTTAGAC TTTATCCTTA TTGTTGTTAG TGTTGTTAAT ATTCGTTGCT TCAGCCCACG    540
GTGCCTTGGT CTCTCCACAA TCAAATGGAG GATCCCCCAA GCAGCTTCAT TACAGAGTGA    600
TATTGGGAAA GTGAGATCCT CTCACCATTT TGCCAAGATA CTCTAAAATG ACATCCAAGT    660
TTACCAGTAG AAAGACACAG GATGCACAGA ATGGGCATGA CCTTCAGCTC ACGAGCACAC    720
CTGGAGAAAT TCAGAACCAG GTTCTGAATC ATCACGATTG CCTTTTGCAT GAAAACATCG    780
GCTGGTGATG TGACTTCTCT TCAGGCCATG AGCCTAACAY CCTGCCGGTT TTCATGCCCG    840
CTGCAGTAAT GGACGTTTGT GTGAAGAAAT GAACTGTGGA GTACAAAA** CTTTGAGTCT    900
TTCCGATTGC TCATTAATTC ACTTTTTTGT TACTTCTTTC CAAAATGGAA GTGCTGAAGC    960
CATGGTCTTT CTGCCCCTCC AAGCTGATGA AGGGAAGCCT TTGCCAATGG CCCATGGAAG   1020
ACACTTGGTT TGAGAAACCC TGCCCACTTC CAAAGACCAA AGAGATTAGG AAAAGCCTGG   1080
CAGTATTCTC CAACTCCAAA CAAGCTCTAG AGTGCTCCAG GAAAAGTTAT ATTCAGTATA   1140
TGAATAAGTG TTATTCTCCA TTATTAATGT GTTCTGAAAA TATATTATGA ATAAATACAT   1200
CACCACACCC AAAAAAAAAA AAAAAAAAAA AAAA
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ACA4 DNA sequence
Gene name: alpha satellite junction DNA sequence
Unigene number: Hs.247946
Probeset Accession #: M21305
Nucleic Acid Accession #: M21305
Coding sequence: 1-165 (predicted start/stop codons underlined)

ATGGAATGGA ATGGAATGGC ATGGAATCGT ATAAAGTGGA ATGGAATCAA CTCGAGTGGA 60
ATGGAATGGA ATGGAATGGA ATGGAATGCA GTACAATGCA ATAGAATGGA ATGGAATGAA 120
CTCGAGTTGA CTGGAATGGA ATGGAATGGA ATGCATTTGA ATTGA

ACG6 DNA sequence
Gene name: intercellular adhesion molecule 2 (ICAM2)
Unigene number: Hs.83733
Probeset Accession #: M32334
Nucleic Acid Accession #: NM_000873
Coding sequence: 63-890 (predicted start/stop codons underlined)

CTAAAGATCT CCCTCCAGGC AGCCCTTGGC TGGTCCCTGC GAGCCCGTGG AGACTGCCAG 60
AGATGTCCTC TTTCGGTTAC AGGACCCTGA CTGTGGCCCT CTTCACCCTG ATCTGCTGTC 120
CAGGATCGGA TGAGAAGGTA TTCGAGGTAC ACGTGAGGCC AAAGAAGCTG GCGGTTGAGC 180
CCAAAGGGTC CCTCGAGGTC AACTGCAGCA CCACCTGTAA CCAGCCTGAA GTGGGTGGTC 240
TGGAGACCTC TCTAAATAAG ATTCTGCTGG ACGAACAGGC TCAGTGGAAA CATTACTTGG 300
TCTCAAACAT CTCCCATGAC ACGGTCCTCC AATGCCACTT CACCTGCTCC GGGAAGCAGG 360
AGTCAATGAA TTCCAACGTC AGCGTGTACC AGCCTCCAAG GCAGGTCATC CTGACACTGC 420
AACCCACTTT GGTGGCTGTG GGCAAGTCCT TCACCATTGA GTGCAGGGTG CCCACCGTGG 480
AGCCCCTGGA CAGCCTCACC CTCTTCCTGT TCCGTGGCAA TGAGACTCTG CACTATGAGA 540
CCTTCGGGAA GGCAGCCCCT GCTCCGCAGG AGGCCACAGC CACATTCAAC AGCACGGCTG 600
ACAGAGAGGA TGGCCACCGC AACTTCTCCT GCCTGGCTGT GCTGGACTTG ATGTCTCGCG 660
GTGGCAACAT CTTTCACAAA CACTCAGCCC CGAAGATGTT GGAGATCTAT GAGCCTGTGT 720
CGGACAGCCA GATGGTCATC ATAGTCACGG TGGTGTCGGT GTTGCTGTCC CTGTTCGTGA 780
CATCTGTCCT GCTCTGCTTC ATCTTCGGCC AGCACTTGCG CCAGCAGCGG ATGGGCACCT 840
ACGGGGTGCG AGCGGCTTGG AGGAGGCTGC CCCAGGCCTT CCGGCCATAG CAACCATGAG 900
TGGCATGGCC ACCACCACGG TGGTCACTGG AACTCAGTGT GACTCCTCAG GGTTGAGGTC 960
CAGCCCTGGC TGAAGGACTG TGACAGGCAG CAGAGACTTG GGACATTGCC TTTTCTAGCC 1020
CGAATACAAA CACCTGGACT T

ACG7 DNA sequence
Gene name: Cadherin 5, VE-cadherin (CDH5)
Unigene number: Hs.76206
Probeset Accession #: X79981
Nucleic Acid Accession #: NM_001795
Coding sequence: 25-2379 (predicted start/stop codons underlined)

GCACGATCTG TTCCTCCTGG GAAGATGCAG AGGCTCATGA TGCTCCTCGC CACATCGGGC 60
GCCTGCCTGG GCCTGCTGGC AGTGGCAGCA GTGGCAGCAG CAGGTGCTAA CCCTGCCCAA 120
CGGGACACCC ACAGCCTGCT GCCCACCCAC CGGCGCCAAA AGAGAGATTG GATTTGGAAC 180
CAGATGCACA TTGATGAAGA GAAAAACACC TCACTTCCCC ATCATGTAGG CAAGATCAAG 240
TCAAGCGTGA GTCGCAAGAA TGCCAAGTAC CTGCTCAAAG GAGAATATGT GGGCAAGGTC 300
TTCCGGGTCG ATGCAGAGAC AGGAGACGTG TTCGCCATTG AGAGGCTGGA CCGGGAGAAT 360
ATCTCAGAGT ACCACCTCAC TGCTGTCATT GTGGACAAGG ACACTGGTGA AAACCTGGAG 420
ACTCCTTCCA GCTTCACCAT CAAAGTTCAT GACGTGAACG ACAACTGGCC TGTGTTCACG 480
CATCGGTTGT TCAATGCGTC CGTGCCTGAG TCGTCGGCTG TGGGGACCTC AGTCATCTCT 540
GTGACAGCAG TGGATGCAGA CGACCCCACT GTGGGAGACC ACGCCTCTGT CATGTACCAA 600
ATCCTGAAGG GGAAAGAGTA TTTTGCCATC GATAATTCTG GACGTATTAT CACAATAACG 660
AAAAGCTTGG ACCGAGAGAA GCAGGCCAGG TATGAGATCG TGGTGGAAGC GCGAGATGCC 720
CAGGGCCTCC GGGGGGACTC GGGCACGGCC ACCGTGCTGG TCACTCTGCA AGACATCAAT 780
GACAACTTCC CCTTCTTCAC CCAGACCAAG TACACATTTG TCGTGCCTGA AGACACCCGT 840
GTGGGCACCT CTGTGGGCTC TCTGTTTGTT GAGGACCCAG ATGAGCCCCA GAACCGGATG 900
ACCAAGTACA GCATCTTGCG GGGCGACTAC CAGGACGCTT TCACCATTGA GACAAACCCC 960
GCCCACAACG AGGGCATCAT CAAGCCCATG AAGCCTCTGG ATTATGAATA CATCCAGCAA 1020
TACAGCTTCA TCGTCGAGGC CACAGACCCC ACCATCGACC TCCGATACAT GAGCCCTCCC 1080
GCGGGAAACA GAGCCCAGGT CATTATCAAC ATCACAGATG TGGACGAGCC CCCCATTTTC 1140
CAGCAGCCTT TCTACCACTT CCAGCTGAAG GAAAACCAGA AGAAGCCTCT GATTGGCACA 1200
GTGCTGGCCA TGGACCCTGA TGCGGCTAGG CATAGCATTG GATACTCCAT CCGCAGGACC 1260
AGTGACAAGG GCCAGTTCTT CCGAGTCACA AAAAAGGGGG ACATTTACAA TGAGAAAGAA 1320

CTGGACAGAG AAGTCTACCC CTGGTATAAC CTGACTGTGG AGGCCAAAGA ACTGGATTCC 1380
ACTGGAACCC CCACAGGAAA AGAATCCATT GTGCAAGTCC ACATTGAAGT TTTGGATGAG 1440
AATGACAATG CCCCGGAGTT TGCCAAGCCC TACCAGCCCA AAGTGTGTGA GAACGCTGTC 1500
CATGGCCAGC TGGTCCTGCA GATCTCCGCA ATAGACAAGG ACATAACACC ACGAAACGTG 1560
AAGTTCAAAT TCACCTTGAA TACTGAGAAC AACTTTACCC TCACGGATAA TCACGATAAC 1620
ACGGCCAACA TCACAGTCAA GTATGGGCAG TTTGACCGGG AGCATACCAA GGTCCACTTC 1680
CTACCCGTGG TCATCTCAGA CAATGGGATG CCAAGTCGCA CGGGCACCAG CACGCTGACC 1740
GTGGCCGTGT GCAAGTGCAA CGAGCAGGGC GAGTTCACCT TCTGCGAGGA TATGGCCGCC 1800
CAGGTGGGCG TGAGCATCCA GGCAGTGGTA GCCATCTTAC TCTGCATCCT CACCATCACA 1860
GTGATCACCC TGCTCATCTT CCTGCGGCGG CGGCTCCGGA AGCAGGCCCG CGCGCACGGC 1920
AAGAGCGTGC CGGAGATCCA CGAGCAGCTG GTCACCTACG ACGAGGAGGG CGGCGGCGAG 1980
ATGGACACCA CCAGCTACGA TGTGTCGGTG CTCAACTCGG TGCGCCGCGG CGGGGCCAAG 2040
CCCCCGCGGC CCGCGCTGGA CGCCCGGCCT TCCCTCTATG CGCAGGTGCA GAAGCCACCG 2100
AGGCACGCGC CTGGGGCACA CGGAGGGCCC GGGGAGATGG CAGCCATGAT CGAGGTGAAG 2160
AAGGACGAGG CGGACCACGA CGGCGACGGC CCCCCCTACG ACACGCTGCA CATCTACGGC 2220
TACGAGGGCT CCGAGTCCAT AGCCGAGTCC CTCAGCTCCC TGGGCACCGA CTCATCCGAC 2280
TCTGACGTGG ATTACGACTT CCTTAACGAC TGGGGACCCA GGTTTAAGAT GCTGGCTGAG 2340
CTGTACGGCT CGGACCCCCG GGAGGAGCTG CTGTATTAGG CGGCCGAGGT CACTCTGGGC 2400
CTGGGGACCC AAACCCCCTG CAGCCCAGGC CAGTCAGACT CCAGGCACCA CAGCCTCCAA 2460
AAATGGCAGT GACTCCCCAG CCCAGCACCC CTTCCTCGTG GGTCCCAGAG ACCTCATCAG 2520
CCTTGGGATA GCAAACTCCA GGTTCCTGAA ATATCCAGGA ATATATGTCA GTGATGACTA 2580
TTCTCAAATG CTGGCAAATC CAGGCTGGTG TTCTGTCTGG GCTCAGACAT CCACATAACC 2640
CTGTCACCCA CAGACCGCCG TCTAACTCAA AGACTTCCTC TGGCTCCCCA AGGCTGCAAA 2700
GCAAAACAGA CTGTGTTTAA CTGCTGCAGG GTCTTTTTCT AGGGTCCCTG AACGCCCTGG 2760
TAAGGCTGGT GAGGTCCTGG TGCCTATCTG CCTGGAGGCA AAGGCCTGGA CAGCTTGACT 2820
TGTGGGGCAG GATTCTCTGC AGCCCATTCC CAAGGGAGAC TGACCATCAT GCCCTCTCTC 2880
GGGAGCCCTA GCCCTGCTCC AACTCCATAC TCCACTCCAA GTGCCCCACC ACTCCCCAAC 2940
CCCTCTCCAG GCCTGTCAAG AGGGAGGAAG GGGCCCCATG GCAGCTCCTG ACCTTGGGTC 3000
CTGAAGTGAC CTCACTGGCC TGCCATGCCA GTAACTGTGC TGTACTGAGC ACTGAACCAC 3060
ATTCAGGGAA ATGCTTATTA AACCTTGAAG CAACTGTGAA TTCATTCTGG AGGGGCAGTG 3120
GAGATCAGGA GTGACAGATC ACAGGGTGAG GGCCACCTCC ACACCCACCC CCTCTGGAGA 3180
AGGCCTGGAA GAGCTGAGAC CTTGCTTTGA GACTCCTCAG CACCCCTCCA GTTTTGCCTG 3240
AGAAGGGGCA GATGTTCCCG GAGATCAGAA GACGTCTCCC CTTCTCTGCC TCACCTGGTC 3300
GCCAATCCAT GCTCTCTTTC TTTTCTCTGT CTACTCCTTA TCCCTTGGTT TAGAGGAACC 3360
CAAGATGTGG CCTTTAGCAA AACTGACAAT GTCCAAACCC ACTCATGACT GCATGACGGA 3420
GCCGAGCATG TGTCTTTACA CCTCGCTGTT GTCACATCTC AGGGAACTGA CCCTCAGGCA 3480
CACCTTGCAG AAGGAAGGCC CTGCCCTGCC CAACCTCTGT GGTCACCCAT GCATCATTCC 3540
ACTGGAACGT TTCACTGCAA ACACACCTTG GAGAAGTGGC ATCAGTCAAC AGAGAGGGGC 3600
AGGGAAGGAG ACACCAAGCT CACCCTTCGT CATGGACCGA GGTTCCCACT CTGGCAAAGC 3660
CCCTCACACT GCAAGGGATT GTAGATAACA CTGACTTGTT TGTTTTAACC AATAACTAGC 3720
TTCTTATAAT GATTTTTTTA CTAATGATAC TTACAAGTTT CTAGCTCTCA CAGACATATA 3780
GAATAAGGGT TTTTGCATAA TAAGCAGGTT GTTATTTAGG TTAACAATAT TAATTCAGGT 3840
TTTTTAGTTG GAAAAACAAT TCCTGTAACC TTCTATTTTC TATAATTGTA GTAATTGCTC 3900
TACAGATAAT GTCTATATAT TGGCCAAACT GGTGCATGAC AAGTACTGTA TTTTTTTATA 3960
CCTAAATAAA GAAAAATCTT TAGCCTGGGC AACAAAAAAA

ACG9 DNA sequence
Gene name: lysyl oxidase-like 2 (LOXL2)
Unigene number: Hs.83354
Probeset Accession #: U89942
Nucleic Acid Accession #: NM_002318 cluster
Coding sequence: 248-2572 (predicted start/stop codons underlined)

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CCGCCCCCTC TGCTCGAGAA AGGGGCTCAG CGGCGGCGGA AGCGGAGGGG GACCACCGTG 120
GAGAGCGCGG TCCCAGCCCG GCCACTGCGG ATCCCTGAAA CCAAAAAGCT CCTGCTGCTT 180
CTGTACCCCG CCTGTCCCTC CCAGCTGCGC AGGGCCCCTT CGTGGGATCA TCAGCCCGAA 240
GACAGGGATG GAGAGGCCTC TGTGCTCCCA CCTCTGCAGC TGCCTGGCTA TGCTGGCCCT 300
CCTGTCCCCC CTGAGCCTGG CACAGTATGA CAGCTGGCCC CATTACCCCG AGTACTTCCA 360
GCAACCGGCT CCTGAGTATC ACCAGCCCCA GGCCCCCGCC AACGTGGCCA AGATTCAGCT 420
GCGCCTGGCT GGGCAGAAGA GGAAGCACAG CGAGGGCCGG GTGGAGGTGT ACTATGATGG 480
CCAGTGGGGC ACCGTGTGCG ATGACGACTT CTCCATCCAC GCTGCCCACG TCGTCTGCCG 540
GGAGCTGGGC TATGTGGAGG CCAAGTCCTG GACTGCCAGC TCCTCCTACG GCAAGGGAGA 600
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CACCTCCAAT GGCTGGGGCG TCACTGACTG CAAGCACACG GAGGATGTCG GTGTGGTGTG 720
CAGCGACAAA AGGATTCCTG GGTTCAAATT TGACAATTCG TTGATCAACC AGATAGAGAA 780
CCTGAATATC CAGGTGGAGG ACATTCGGAT TCGAGCCATC CTCTCAACCT ACCGCAAGCG 840

CACCCCAGTG ATGGAGGGCT ACGTGGAGGT GAAGGAGGGC AAGACCTGGA AGCAGATCTG 900
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CTGGCCATTC TCCATGGACT GCACCGGCAC AGAGGCCCAC ATCTCCAGCT GCAAGCTGGG 1080
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GTCGGCCAGT GTGGTCTGCA GAGAGCTGGG CTTTGGGAGT GCCAAAGAGG CAGTCACTGG 1380
CTCCCGACTG GGGCAAGGGA TCGGACCCAT CCACCTCAAC GAGATCCAGT GCACAGGCAA 1440
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CGGCGGCCGC AATCCCTACG AGGGCCGAGT GGAGGTGCTG GTGGAGAGAA ACGGGTCCCT 1620
TGTGTGGGGG ATGGTGTGTG GCCAAAACTG GGGCATCGTG GAGGCCATGG TGGTCTGCCG 1680
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GGCCGGAGTT GCCTGCTCAG AAACCGCCCC TGACCTGGTC CTCAATGCGG AGATGGTGCA 1920
GCAGACCACC TACCTGGAGG ACCGGCCCAT GTTCATGCTG CAGTGTGCCA TGGAGGAGAA 1980
CTGCCTCTCG GCCTCAGCCG CGCAGACCGA CCCCACCACG GGCTACCGCC GGCTCCTGCG 2040
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ACACGTGGAC AAATGCGGGC TCATCAGCCC CCCCAGAGAG GGTCAGGCCG AACCCCATTT 3000
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CCTCCAGTCT ATTATAGTCA CATAGATAAT GGTGCCACGT GTTTTCTGAT TTGGTGAGCT 3120
CAGACTTGGT GCTTCCCTCT CCACAACCCC CACCCCTTGT TTTTCAAGAT ACTATTATTA 3180
TATTTTCACA GACTTTTGAA GCACAAATTT ATTGGCATTT AATATTGGAC ATCTGGGCCC 3240
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TTCCAATTCT GTGGGTTTTT GATTCAACGG TGCTATAACC AGGGTCCTGG GTGACAGGGC 3360
GCTCACTGAG CACCATGTGT CATCACAGAC ACTTACACAT ACTTGAAACT TGGAATAAAA 3420
GAAAGATTTA TG

ACH2 DNA sequence
Gene name: TIE tyrosine protein kinase
Unigene number: Hs.78824
Probeset Accession #: X60957
Nucleic Acid Accession #: NM_005424 cluster
Coding sequence: 37-3452 (predicted start/stop codons underlined)

CGCTCGTCCT GGCTGGCCTG GGTCGGCCTC TGGAGTATGG TCTGGCGGGT GCCCCCTTTC 60
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GGGGCGGGGA GGGGCTCGGA CGCCTGGGGC CCGCCCCTGC TGCTGGAGAA GGACGACCGT 240
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ACGCTTCGCG GCTTCTCCAA GCCCTCGGAC CTCGTGGGCG TCTTCTCCTG CGTGGGCGGT 360
GCTGGGGCGC GGCGCACGCG CGTCATCTAC GTGCACAACA GCCCTGGAGC CCACCTGCTT 420
CCAGACAAGG TCACACACAC TGTGAACAAA GGTGACACCG CTGTACTTTC TGCACGTGTG 480
CACAAGGAGA AGCAGACAGA CGTGATCTGG AAGAGCAACG GATCCTACTT CTACACCCTG 540
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TCGAGCGGCA TCTACAGTGC CACTTACCTG GAAGCCAGCC CCCTGGGCAG CGCCTTCTTT 660
CGGCTCATCG TGCGGGGTTG TGGGGCTGGG CGCTGGGGGC CAGGCTGTAC CAAGGAGTGC 720
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CAGGAGCAGT GCCCAGGCAT ATCAGGCTGC CGGGGCCTCA CCTTCTGCCT CCCAGACCCC 900

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GAGGGGGCCT GGGGGCCTCC CACCCTCATG ACCACAGACT GTCCTGAGCC TTTGTTGCAG 1680
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CGGGGGCAGG AGCGGCGGGA GAACGTCTCA TCCCCCCAGG CCCGCACTGC CCTCCTGACG 1860
GGACTCACGC CTGGCACCCA CTACCAGCTG GATGTGCAGC TCTACCACTG CACCCTCCTG 1920
GGCCCGGCCT CGCCCCCTGC ACACGTGCTT CTGCCCCCCA GTGGGCCTCC AGCCCCCCGA 1980
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GCTCTGCCTG GGCCAATATC CAAGTACGTT GTGGAGGTGC AGGTGGCTGG GGGTGCAGGA 2100
GACCCACTGT GGATAGACGT GGACAGGCCT GAGGAGACAA GCACCATCAT CCGTGGCCTC 2160
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GCTGGCCGGA GCAAACTCTG CTGTCTAACC TGTGACCAGT CTGACCCTTA CAGCCTCTGA 3540
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GGTGGGCTTA GGGGAACTGG GTTCCCATGC TTTGTAGGTG TCTCATAGCT ATCCTGGGCA 3660
TCCTTCTTTC TAGTTCAGCT GCCCCACAGG TGTGTTTCCC ATCCCACTGC TCCCCCAACA 3720
CAAACCCCCA CTCCAGCTCC TTCGCTTAAG CCAGCACTCA CACCACTAAC ATGCCCTGTT 3780
CAGCTACTCC CACTCCCGGC CTGTCATTCA GAAAAAAATA AATGTTCTAA TAAGCTCCAA 3840
AAAAA

ACH3 DNA sequence
Gene name: placental growth factor (PGF; PlGF1; VEGF-related protein)
Unigene number: Hs.2894
Probeset Accession #: X54936
Nucleic Acid Accession #: NM_002632 cluster
Coding sequence: 322-768 (predicted start/stop codons underlined)

GGGATTCGGG CCGCCCAGCT ACGGGAGGAC CTGGAGTGGC ACTGGGCGCC CGACGGGCA 60
TCCCCGGGAC CCGCCTGCCC CTCGGCGCCC CGCCCCGCCG GGCCGCTCCC CGTCGGCTC 120
CCCAGCCACA GCCTTACCTA CGGGCTCCTG ACTCCGCAAG GCTTCCAGAA GATGCTCGAA 180
CCACCGGCCG GGGCCTCGGG GCAGCAGTGA GGGAGGCGTC CAGCCCCCCA CTCAGCTCTT 240
CTCCTCCTGT GCCAGGGGCT CCCCGGGGGA TGAGCATGGT GGTTTTCCCT CGGAGCCCCC 300
TGGCTCGGGA CGTCTGAGAA GATGCCGGTC ATGAGGCTGT TCCCTTGCTT CCTGCAGCTC 360
CTGGCCGGGC TGGCGCTGCC TGCTGTGCCC CCCCAGCAGT GGGCCTTGTC TGCTGGGAAC 420
GGCTCGTCAG AGGTGGAAGT GGTACCCTTC CAGGAAGTGT GGGGCCGCAG CTACTGCCGG 480
GCGCTGGAGA GGCTGGTGGA CGTCGTGTCC GAGTACCCCA GCGAGGTGGA GCACATGTTC 540

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AGCCCATCCT GTGTCTCCCT GCTGCGCTGC ACCGGCTGCT GCGGCGATGA GAATCTGCAC   600
TGTGTGCCGG TGGAGACGGC CAATGTCACC ATGCAGCTCC TAAAGATCCG TTCTGGGGAC   660
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CGGGAGAAGA TGAAGCCGGA AAGGTGCGGC GATGCTGTTC CCCGGAGGTA ACCCACCCCT   780
TGGAGGAGAG AGACCCCGCA CCCGGCTCGT GTATTTATTA CCGTCACACT CTTCAGTGAC   840
TCCTGCTGGT ACCTGCCCTC TATTTATTAG CCAACTGTTT CCCTGCTGAA TGCCTCGCTC   900
CCTTCAAGAC GAGGGGCAGG GAAGGACAGG ACCCTCAGGA ATTCAGTGCC TTCAACAACG   960
TGAGAGAAAG AGAGAAGCCA GCCACAGACC CCTGGGAGCT TCCGCTTTGA AAGAAGCAAG  1020
ACACGTGGCC TCGTGAGGGG CAAGCTAGGC CCCAGAGGCC CTGGAGGTCT CCAGGGGCCT  1080
GCAGAAGGAA AGAAGGGGGC CCTGCTACCT GTTCTTGGGC CTCAGGCTCT GCACAGACAA  1140
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ACGGCCTGGT GGTGGGAAGG CCGGCAGCGG GCGGAGGGGA TTCAGCCACT TCCCCCTCTT  1260
CTTCTGAAGA TCAGAACATT CAGCTCTGGA GAACAGTGGT TGCCTGGGGG CTTTTGCCAC  1320
TCCTTGTCCC CCGTGATCTC CCCTCACACT TTGCCATTTG CTTGTACTGG GACATTGTTC  1380
TTTCCGGCCG AGGTGCCACC ACCCTGCCCC CACTAAGAGA CACATACAGA GTGGGCCCCG  1440
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GGGAGGAGCC TGTGCGTCCC AGCTGAAGGC AGTGGCAGGG GAGCAGGTTC CCCAAGGGCC  1560
CTGGCACCCC CACAAGCTGT CCCTGCAGGG CCATCTGACT GCCAAGCCAG ATTCTCTTGA  1620
ATAAAGTATT CTAGTGTGGA AACGC
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ACH4 DNA sequence
Gene name: nidogen 2 (NID2)
Unigene number: Hs.82733
Probeset Accession #: D86425
Nucleic Acid Accession #: NM_007361 cluster
Coding sequence: 1-4131 (predicted start/stop codons underlined)

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GAGTCGTGGT GGGACCAGCT CCTGCAGGAA GGCGACGACG TAAAGCTCAG CCGTGGTGAA   180
GCTGGCGAAT CCCCTGCACT TCTTACGAAG CCCGATTCAG CAACCTCTAC GTGGGCACCA   240
ACGGCATCAT CTCCACTCAG GACTTCCCCA GGGAAACGCA GTATGTGGAC TATGATTTCC   300
CCACCGACTT CCCGGCCATC GCCCCTTTTC TGGCGGACAT CGACACGAGC CACGGCAGAG   360
GCCGAGTCCT GTACCGAGAG GACACCTCCC CCGCAGTGCT GGGCCTGGCC GCCCGCTATG   420
TGCGCGCTGG CTTCCCGCGC TCTGCGCGCT TTTTACCCCC ACCCACGCCT TCCTGGCCAC   480
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CTTAGATTTG CTGTGACCAA TCAAATTGGC CCGGTCAAAG AAGATTCAGA CCCCACTCCG  2280
GTGAATCCTT GCTATGATGG GAGCCACATG TGTGACACAA CAGCACGGTG CCATCCAGGG  2340
ACAGGTGTAG ATTACACCTG TGAGTGCGCA TCTGGGTACC AGGGAGATGG ACGGAACTGT  2400
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GTGGATGAAA ATGAATGTGC AACTGGCTTT CATCGCTGTG GCCCCAACTC TGTATGTATC 2460
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GATGTGACCC CTCCATCTGT GGGCACCTTC CTGCTCTATA CTCAGGGCCA GCAGATTGGC 3360
TACTTACCCC TCAATGGCAC CAGGCTTCAG AAGGATGCAG CTAAGACCCT GCTGTCTCTG 3420
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GATGTTGCTG GACGGACAAT CAGCCGTGCC GGTCTGGAAC TGGGAGCAGA GCCTGAGACG 3540
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ATTAAAGCAC ATGTGATCAA TATAACAATA TAATCCTAAA CCTTGACAGT TGGAGAAGCC 4560
AATGCAGAAC TGATGGGAAA GGACCAATTA TTTATAGTTT CCCAACAAAA GTTCTAAGAT 4620
TTTTTACCTC TGCATCAGTG CATTTCTATT TATATCAAAA GGTGCTAAAA TGATTCAATT 4680
TGCATTTTCT GATCCTGTAG TGCCTCTATA GAAGTACCCA CAGAAAGTAA AGTATCACAT 4740
TTATAAATAC CAAAGATGTA ACAATTTTAA AATTTTCTAG ATTACTCCAA TAAAGTGTTT 4800
TAAGTTTAAA AAAAAAAAAA AAAAAAAAA

ACH5 DNA sequence
Gene name: SNL (singed-like; sea urchin fascin homolog-like)
Unigene number: Hs.118400
Probeset Accession #: 003057
Nucleic Acid Accession #: NM_003088
Coding sequence: 112-1593 (predicted start/stop codons underlined)

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CTGACGGCCG AGGCGTTCGG GTTCAAGGTG AACGCGTCCG CCAGCAGCCT GAAGAAGAAG 240
CAGATCTGGA CGCTGGAGCA GCCCCCTGAC GAGGCGGGCA GCGCGGCCGT GTGCCTGCGC 300
AGCCACCTGG GCCGCTACCT GGCGGCGGAC AAGGACGGCA ACGTGACCTG CGAGCGCGAG 360
GTGCCCGGTC CCGACTGCCG TTTCCTCATC GTGGCGCACG ACGACGGTCG CTGGTCGCTG 420
CAGTCCGAGG CGCACCGGCG CTACTTCGGC GGCACCGAGG ACCGCCTGTC CTGCTTCGCG 480
CAGACGGTGT CCCCCGCCGA GAAGTGGAGC GTGCACATCG CCATGCACCC TCAGGTCAAC 540
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CGCGACTGCG AGGGCCGTTA CCTGGCGCCG TCGGGGCCCA GCGGCACGCT CAAGGCGGGC 840
AAGGCCACCA AGGTGGGCAA GGACGAGCTC TTTGCTCTGG AGCAGAGCTG CGCCCAGGTC 900
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GCCGCCTCGG TGGAGACAGC AGGGGACTCA GAGCTCTTCC TCATGAAGCT CATCAACCGC 1260
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AGTCTGC

ACH6 DNA sequence
Gene name: endothelial protein C receptor (EPCR; PROCR)
Unigene number: Hs.82353
Probeset Accession #: L35545
Nucleic Acid Accession #: NM_006404
Coding sequence: 25-741 (predicted start/stop codons underlined)

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AATATTAATA AATTTCTTAT ATTT

ACH8 DNA sequence
Gene name: melanoma adhesion molecule (MCAM; MUC18)
Unigene number: Hs.211579
Probeset Accession #: D51069
Nucleic Acid Accession #: NM_006500
Coding sequence: 27-1967 (predicted start and stop codons underlined)

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TTGTTTCCTT TATATATGTA TGTATATATA TATATGAAAA TATATATATA TATGAAAAAT 3300
AAAGCTTAAT TGTCCCAGAA AATCATACAT TGCTTTTTTA TTCTACATGG GTACCACAGG 3360
AACCTGGGGG CCTGTGAAAC TACAACCAAA AGGCACACAA AACCGTTTCC AGTTGGCAGC 3420
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CTACCCTACT TTTCAGCAGC AAAACGTCCC GTATGACGCA GCACGAAGGG CCTGGCAGGC 3540
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ACH9 DNA Sequence
Gene name: endothelin-1 (EDN1)
Unigene number: Hs.2271
Probeset Accession #: J05008
Nucleic Acid Accession #: NM_001955

Coding sequence: 337-975 (predicted start/stop codons underlined)

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AGGCGCTGCC TTTTCTCCCC GTTAAAGGGC ACTTGGGCTG AAGGATCGCT TTGAGATCTG   240
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TTCCTGACTG GCAAAGGACC AGCGTCCTCG TTCAAAACAT TCCAAGAAAG GTTAAGGAGT  1140
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ACJ1 DNA sequence
Gene name: BMX non-receptor tyrosine kinase
Unigene number: Hs.27372
Probeset Accession #: X83107
Nucleic Acid Accession #: NM_001721
Coding sequence: 34-2061 (predicted start/stop codons underlined)

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ACJ4 DNA sequence
Gene name: prostaglandin G/H synthase 2 (COX-2; PGHS-2)
Unigene number: Hs.196384
Probeset Accession #: D28235
Nucleic Acid Accession #: NM_000963
Coding sequence: 135-1949 (predicted start/stop codons underlined)

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ACJ6 DNA sequence
Gene name: SEC14-like-1
Unigene number: Hs.75232
Probeset Accession #: D67029
Nucleic Acid Accession #: NM_003003
Coding sequence: 304-2451 (predicted start/stop codons underlined)

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AGJ8 DNA sequence
Gene name: intercellular adhesion molecule 1 (ICAM1; CD54)
Unigene number: Hs.168383
Probeset Accession #: M24283
Nucleic Acid Accession #: NM_000201
Coding sequence: 58-1656 (predicted start/stop codons underlined)

GCGCCCCAGT CGACGCTGAG CTCCTCTGCT ACTCAGAGTT GCAACCTCAG CCTCGCTATG 60
GCTCCCAGCA GCCCCCGGCC CGCGCTGCCC GCACTCCTGG TCCTGCTCGG GGCTCTGTTC 120
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GGCTCCGTGC TGGTGACATG CAGCACCTCC TGTGACCAGC CCAAGTTGTT GGGCATAGAG 240
ACCCCGTTGC CTAAAAAGGA GTTGCTCCTG CCTGGGAACA ACCGGAAGGT GTATGAACTG 300
AGCAATGTGC AAGAAGATAG CCAACCAATG TGCTATTCAA ACTGCCCTGA TGGGCAGTCA 360

ACAGCTAAAA CCTTCCTCAC CGTGTACTGG ACTCCAGAAC GGGTGGAACT GGCACCCCTC 420
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CCCCGGGCCA ACCTCACCGT GGTGCTGCTC CGTGGGGAGA AGGAGCTGAA ACGGGAGCCA 540
GCTGTGGGGG AGCCCGCTGA GGTCACGACC ACGGTGCTGG TGAGGAGAGA TCACCATGGA 600
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CTGTTCCCAG TCTCGGAGGC CCAGGTCCAC CTGGCACTGG GGGACCAGAG GTTGAACCCC 840
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GACGAGGGCA CCCAGCGGCT GACGTGTGCA GTAATACTGG GGAACCAGAG CCAGGAGACA 960
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GTCTCAGAAG GGACCGAGGT GACAGTGAAG TGTGAGGCCC ACCCTAGAGC CAAGGTGACG 1080
CTGAATGGGG TTCCAGCCCA GCCACTGGGC CCGAGGGCCC AGCTCCTGCT GAAGGCCACC 1140
CCAGAGGACA ACGGGCGCAG CTTCTCCTGC TCTGCAACCC TGGAGGTGGC CGGCCAGCTT 1200
ATACACAAGA ACCAGACCCG GGAGCTTCGT GTCCTGTATG GCCCCCGACT GGACGAGAGG 1260
GATTGTCCGG GAAACTGGAC GTGGCCAGAA AATTCCCAGC AGACTCCAAT GTGCCAGGCT 1320
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ACK3 DNA sequence
Gene name: angiopoietin 1 receptor (TIE-2; TEK)
Unigene number: Hs.89640
Probeset Accession #: L06139
Nucleic Acid Accession #: NM_000459
Coding sequence: 149-3523 (predicted start/stop codons underlined)

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CCTACCTCTT GTATCTGATG CTGAAACATC TCTCACCTGC ATTGCCTCTG GGTGGCGCCC 300
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CAGGTATATA GGAGGAAACC TCTTCACCTC GGCCTTCACC AGGCTGATAG TCCGGAGATG 780
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AGCTTCTGGC TGGCCGCTAC CTACTAATGA AGAAATGACC CTGGTGAAGC CGGATGGGAC 1320
AGTGCTCCAT CCAAAAGACT TTAACCATAC GGATCATTTC TCAGTAGCCA TATTCACCAT 1380
CCACCGGATC CTCCCCCCTG ACTCAGGAGT TTGGGTCTGC AGTGTGAACA CAGTGGCTGG 1440
GATGGTGGAA AAGCCCTTCA ACATTTCTGT TAAAGTTCTT CCAAAGCCCC TGAATGCCCC 1500
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GCACATTGTA AAAAGTTTTA GTTTTGATGA GTTGTGAGTT TACCTTGTAT ACTGTAGGCA 4080
CACTTTGCAC TGATATATCA TGAGTGAATA AATGTCTTGC CTACTCAAAA AAAAAAAA

PZA6 DNA sequence
Gene name: prostate differentiation factor (PLAB; MIC-1)
Unigene number: Hs.116577
Probeset Accession #: AB000584
Nucleic Acid Accession #: NM_004864
Coding sequence: 26-952 (predicted start/stop codons underlined)

CGGAACGAGG GCAACCTGCA CAGCCATGCC CGGGCAAGAA CTCAGGACGG TGAATGGCTC 60
TCAGATGCTC CTGGTGTTGC TGGTGCTCTC GTGGCTGCCG CATGGGGGCG CCCTGTCTCT 120
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AAC8 DNA sequence
Gene name: none
Unigene number: Hs.6682
Probeset Accession #: AA227926
Nucleic Acid Accession #: none
Coding sequence: no ORF identified, possible frameshifts

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AAD2 DNA sequence
Gene name: Thrombospondin-1
Unigene number: Hs.87409
Probeset Accession #: AA232645
Nucleic Acid Accession #: NM_003246
Coding sequence: 112-3624 (predicted start/stop codons underlined)

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GACTATGACA GAGATGATGT GGGAGACCGC TGTGACAACT GTCCCTACAA CCACAACCCA  2460
GATCAGGCAG ACACAGACAA CAATGGCGAA GGAGACGCCT GTGCTGCAGA CATTGATGGA  2520
GACGGTATCC TCAATGAACG GGACAACTGC CAGTACGTCT ACAATGTGGA CCAGAGAGAC  2580
ACTGATATGG ATGGGGTTGG AGATCAGTGT GACAATTGCC CCTTGGAACA CAATCCGGAT  2640
CAGCTGGACT CTGACTCAGA CCGCATTGGA GATACCTGTG ACAACAATCA GGATATTGAT  2700
GAAGATGGCC ACCAGAACAA TCTGGACAAC TGTCCCTATG TGCCCAATGC CAACCAGGCT  2760
GACCATGACA AAGATGGCAA GGGAGATGCC TGTGACCACG ATGATGACAA CGATGGCATT  2820
CCTGATGACA AGGACAACTG CAGACTCGTG CCCAATCCCG ACCAGAAGGA CTCTGACGGC  2880
GATGGTCGAG GTGATGCCTG CAAAGATGAT TTTGACCATG ACAGTGTGCC AGACATCGAT  2940
GACATCTGTC CTGAGAATGT TGACATCAGT GAGACCGATT TCCGCCGATT CCAGATGATT  3000
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CCTCTGGACC CCAAAGGGAC ATCCCAAAAT GACCCTAACT GGGTTGTACG CCATCAGGGT 3060
AAAGAACTCG TCCAGACTGT CAACTGTGAT CCTGGACTCG CTGTAGGTTA TGATGAGTTT 3120
AATGCTGTGG ACTTCAGTGG CACCTTCTTC ATCAACACCG AAAGGGACGA TGACTATGCT 3180
GGATTTGTCT TTGGCTACCA GTCCAGCAGC CGCTTTTATG TTGTGATGTG GAAGCAAGTC 3240
ACCCAGTCCT ACTGGGACAC CAACCCCACG AGGGCTCAGG GATACTCGGG CCTTTCTGTG 3300
AAAGTTGTAA ACTCCACCAC AGGGCCTGGC GAGCACCTGC GGAACGCCCT GTGGCACACA 3360
GGAAACACCC CTGGCCAGGT GCGCACCCTG TGGCATGACC CTCGTCACAT AGGCTGGAAA 3420
GATTTCACCG CCTACAGATG GCGTCTCAGC CACAGGCCAA AGACGGGTTT CATTAGAGTG 3480
GTGATGTATG AAGGGAAGAA AATCATGGCT GACTCAGGAC CCATCTATGA TAAAACCTAT 3540
GCTGGTGGTA GACTAGGGTT GTTTGTCTTC TCTCAAGAAA TGGTGTTCTT CTCTGACCTG 3600
AAATACGAAT GTAGAGATCC CTAATCATCA AATTGTTGAT TGAAAGACTG ATCATAAACC 3660
AATGCTGGTA TTGCACCTTC TGGAACTATG GGCTTGAGAA AACCCCCAGG ATCACTTCTC 3720
CTTGGCTTCC TTCTTTTCTG TGCTTGCATC AGTGTGGACT CCTAGAACGT GCGACCTGCC 3780
TCAAGAAAAT GCAGTTTTCA AAAACAGACT CATCAGCATT CAGCCTCCAA TGAATAAGAC 3840
ATCTTCCAAG CATATAAACA ATTGCTTTGG TTTCCTTTTG AAAAAGCATC TACTTGCTTC 3900
AGTTGGGAAG GTGCCCATTC CACTCTGCCT TTGTCACAGA GCAGGGTGCT ATTGTGAGGC 3960
CATCTCTGAG CAGTGGACTC AAAAGCATTT TCAGGCATGT CAGAGAAGGG AGGACTCACT 4020
AGAATTAGCA AACAAAACCA CCCTGACATC CTCCTTCAGG AACACGGGGA GCAGAGGCCA 4080
AAGCACTAAG GGGAGGGCGC ATACCCGAGA CGATTGTATG AAGAAAATAT GGAGGAACTG 4140
TTACATGTTC GGTACTAAGT CATTTTCAGG GGATTGAAAG ACTATTGCTG GATTTCATGA 4200
TGCTGACTGG CGTTAGCTGA TTAACCCATG TAAATAGGCA CTTAAATAGA AGCAGGAAAG 4260
GGAGACAAAG ACTGGCTTCT GGACTTCCTC CCTGATCCCC ACCCTTACTC ATCACCTTGC 4320
AGTGGCCAGA ATTAGGGAAT CAGAATCAAA CCAGTGTAAG GCAGTGCTGG CTGCCATTGC 4380
CTGGTCACAT TGAAATTGGT GGCTTCATTC TAGATGTAGC TTGTGCAGAT GTAGCAGGAA 4440
AATAGGAAAA CCTACCATCT CAGTGAGCAC CAGCTGCCTC CCAAAGGAGG GGCAGCCGTG 4500
CTTATATTTT TATGGTTACA ATGGCACAAA ATTATTATCA ACCTAACTAA AACATTCCTT 4560
TTCTCTTTTT TCCGTAATTA CTAGGTAGTT TTCTAATTCT CTCTTTTGGA AGTATGATTT 4620
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ATTTGCAAAT GTTTTAAATT GCAAAGAAAG CCATGAGGTC TTCAATACTG TTTTACCCCA 5040
TCCCTTGTGC ATATTTCCAG GGAGAAGGAA AGCATATACA CTTTTTTCTT TCATTTTTCC 5100
AAAAGAGAAA AAAATGACAA AAGGTGAAAC TTACATACAA ATATTACCTC ATTTGTTGTG 5160
TGACTGAGTA AAGAATTTTT GGATCAAGCG GAAAGAGTTT AAGTGTCTAA CAAACTTAAA 5220
GCTACTGTAG TACCTAAAAA GTCAGTGTTG TACATAGCAT AAAAACTCTG CAGAGAAGTA 5280
TTCCCAATAA GGAAATAGCA TTGAAATGTT AAATACAATT TCTGAAAGTT ATGTTTTTTT 5340
TCTATCATCT GGTATACCAT TGCTTTATTT TTATAAATTA TTTTCTCATT GCCATTGGAA 5400
TAGAATATTC AGATTGTGTA GATATGCTAT TTAAATAATT TATCAGGAAA TACTGCCTGT 5460
AGAGTTAGTA TTTCTATTTT TATATAATGT TTGCACACTG AATTGAAGAA TTGTTGGTTT 5520
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CTATTTGCCA ATACCTTTTT CTAGGAATGT GCTTTTTTTT GTACACATTT TTATCCATTT 5640
TACATTCTAA AGCAGTGTAA GTTGTATATT ACTGTTTCTT ATGTACAAGG AACAACAATA 5700
AATCATATGG AAATTTATAT TT

AAD9 DNA sequence
Gene name: LIM homeobox protein cofactor (CLIM-1)
Unigene number: Hs.4980
Probeset Accession #: F13782
Nucleic Acid Accession #: AF047337
Coding sequence: 110-1231(predicted start/stop codons underlined)

GTGAGCGTGT GTGCGTGCGT CTACTTTGTA CTGGGAAGAA CACAGCCCAT GTGCTCTGCA 60
TGGACGTTAC TGATACTCTG TTTAGCTTGA TTTTCGAAAA GCAGGCAAGA TGTCCAGCAC 120
ACCACATGAC CCCTTCTATT CTTCTCCTTT CGGCCCATTT TATAGGAGGC ATACACCATA 180
CATGGTACAG CCAGAGTACC GAATCTATGA GATGAACAAG AGACTGCAGT CTCGCACAGA 240
GGATAGTGAC AACCTCTGGT GGGACGCCTT TGCCACTGAA TTTTTTGAAG ATGACGCCAC 300
ATTAACCCTT TCATTTTGTT TGGAAGATGG ACCAAAGCGA TACACTATCG GCAGGACCCT 360
CATCCCCCGT TACTTTAGCA CTGTGTTTGA AGGAGGGGTG ACCGACCTGT ATTACATTCT 420
CAAACACTCG AAAGAGTCAT ACCACAACTC ATCCATCACG GTGGACTGCG ACCAGTGTAC 480
CATGGTCACC CAGCACGGGA AGCCCATGTT TACCAAGGTA TGTACAGAAG GCAGACTGAT 540
CTTGGAGTTC ACCTTTGATG ATCTCATGAG AATCAAAACA TGGCACTTTA CCATTAGACA 600
ATACCGAGAG TTAGTCCCGA GAAGCATCCT AGCCATGCAT GCACAAGATC CTCAGGTCCT 660
GGATCAGCTG TCCAAAAACA TCACCAGGAT GGGGCTAACA AACTTCACCC TCAACTACCT 720
CAGGTTGTGT GTAATATTGG AGCCAATGCA GGAACTGATG TCGAGACATA AAACTTACAA 780

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CCTCAGTCCC CGAGACTGCC TGAAGACCTG CTTGTTTCAG AAGTGGCAGA GGATGGTGGC   840
TCCGCCAGCA GAACCCACAA GGCAACCAAC AACCAAACGG AGAAAAAGGA AAAATTCCAC   900
CAGCAGCACT TCCAACAGCA GCGCTGGGAA CAATGCAAAC AGCACTGGCA GCAAGAAGAA   960
GACCACAGCT GCAAACCTGA GTCTGTCCAG TCAGGTACCT GATGTGATGG TGGTAGGAGA  1020
GCCAACTCTG ATGGGAGGTG AGTTTGGGGA CGAGGACGAA AGGCTAATCA CTAGATTAGA  1080
AAACACGCAA TATGATGCGG CCAACGGCAT GGACGACGAG GAGGACTTCA ACAATTCACC  1140
CGCGCTGGGG AACAACAGCC CGTGGAACAG TAAACCTCCC GCCACTCAAG AGACCAAATC  1200
AGAAAACCCC CCACCCCAGG CTTCCCAATA AGATGATCGG CACCAGAATC CACTGTCAAT  1260
AGGCCCGTGG GTGATCATTA CAATTGCAAA TCTTTACTTA CAGGAGAGGA AACAGAAGAG  1320
ATAAAAACTT TTCCATGCAA ATATCTATTT CTAAACCACA ATGATCTGAT TTTCTTTCTT  1380
CTTTCTTTTT TTCTAATTGA GAGGATTATT CCCAGTAAGC TTCCATGACC CTTTCTTGGA  1440
GGCCTTCACA GGTAATACAG ATACTGGCAC TGATTGTAAT TAAAATGAGA GAAAACTCTA  1500
GCGCATCTTC TGGCACGGTT TTAACAACGT GTTTGTGTTG AATTTCCTTT TTATGCATCA  1560
AACGAAGGCC ATATTGTCCA TAAATGCTCA GTGCTCAGGA TCTCATTAAT ATGCCGAACC  1620
TAACTACAGA TGACTTTTTA ATATTGTAAA ATATTTTCTG CTTTTTGACT TGCATCTGAG  1680
AGTTTCTTGT TTCAGTAAAA AAAGAAAAGA CAAAAAAATC AGCTTTGGAA AGTAATTTAA  1740
ATGTACCTTA TTTTTTTTTT CTTTATGTTT TCTTTCATTG GGCAACAGCT AAGAGGGCCC  1800
AGCAAGGTAA TTTATGGTTG AGCTGATGTC AATTGGTTCT TGTCTTGAGT CGACTCAATT  1860
TAGCCCAAGT GCTGAAACAA GAAATGTCAT TTTTTTCATC AAAGACACCA GGGCAGATTT  1920
TTAAGTAAAG AAAGACAATT GGACCCTTAA GAATTTATGC ATTTGTAAAG TTGCTGTTGA  1980
TCCAAATATT TTCAAGCCAT GTAATCCATT GGTTTTGTGG GCAGTTTAAT AAACCTGAAC  2040
CTTTGTGTGT TTTCTAATTG TACCTGAGTT GACCATCCTT TCTTTTTATA GTATATTTCT  2100
TGTATGATAT TTTGTAAAGC TCTCACCTGG TTCTTTTATG GGGACTTTTC GTTTTTGGGC  2160
AACTCCAGTG TATTTATGTG AAACTTTATA AGAGAATTAA TTTTTCCATT TGCATATTAA  2220
TATGTTCCTC CACACATGTA AAGGCACAGT GGCTCCGTGT GTTAAAAAAC AGCTGTATTT  2280
TATGTATGCT TTACTGATAA GTGTGCCAAT AATAAACTGT GTTAATGACC
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AAE1 DNA sequence
Gene name: guanine nucleotide binding protein 11
Unigene number: Hs.83381
Probeset Accession #: U31384
Nucleic Acid Accession #: NM_004126.1
Coding sequence: 108-329 (predicted start/stop codons underlined)

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GGCACGAGCT CGTGCCGGCC TTCAGTTGTT TCGGGACGCG CCGAGCTTCG CCGCTCTTCC    60
AGCGGCTCCG CTGCCAGAGC TAGCCCGAGC CCGGTTCTGG GGCGAAAATG CCTGCCCTTC   120
ACATCGAAGA TTTGCCAGAG AAGGAAAAAC TGAAAATGGA AGTTGAGCAG CTTCGCAAAG   180
AAGTGAAGTT GCAGAGACAA CAAGTGTCTA AATGTTCTGA AGAAATAAAG AACTATATTG   240
AAGAACGTTC TGGAGAGGAT CCTCTAGTAA AGGGAATTCC AGAAGACAAG AACCCCTTTA   300
AAGAAAAAGG CAGCTGTGTT ATTTCATAAA TAACTTGGGA GAAACTGCAT CCTAAGTGGA   360
AGAACTAGTT TGTTTTAGTT TTCCCAGATA AAACCAACAT GCTTTTTAAG GAAGGAAGAA   420
TGAAATTAAA AGGAGACTTT CTTAAGCACC ATATAGATAG GGTTATGTAT AAAAGCATAT   480
GTGCTACTCA TCTTTGCTCA CTATGCAGTC TTTTTTAAGA GAGCAGAGAG TATCAGATGT   540
ACAATTATGG AAATAAGAAC ATTACTTGAG CATGACACTT CTTTCAGTAT ATTGCTTGAT   600
GCTTCAAATA AAGTTTTGTC TT
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AAE2 DNA sequence
Gene name: Transcription factor 4 (immunoglobulin transcription factor 2)(ITF-2) (SL3-3 Enhancer factor 2) (SEF-2)
Unigene number: Hs.289068
Probeset Accession #: M74719
Nucleic Acid Accession #: NM_003199.1
Coding sequence: 200-2203 (predicted start/stop codons underlined)

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CGGGGGGATC TTGGCTGTGT GTCTGCGGAT CTGTAGTGGC GGCGGCGGCG GCGGCGGCGG    60
GGAGGCAGCA GGCGCGGGAG CGGGCGCAGG AGCAGGCGGC GGCGGTGGCG GCGGCGGTTA   120
GACATGAACG CCGCCTCGGC GCCGGCGGTG CACGGAGAGC CCCTTCTCGC GCGCGGGCGG   180
TTTGTGTGAT TTTGCTAAAA TGCATCACCA ACAGCGAATG GCTGCCTTAG GGACGGACAA   240
AGAGCTGAGT GATTTACTGG ATTTCAGTGC GATGTTTTCA CCTCCTGTGA GCAGTGGGAA   300
AAATGGACCA ACTTCTTTGG CAAGTGGACA TTTTACTGGC TCAAATGTAG AAGACAGAAG   360
TAGCTCAGGG TCCTGGGGGA ATGGAGGACA TCCAAGCCCG TCCAGGAACT ATGGAGATGG   420
GACTCCCTAT GACCACATGA CCAGCAGGGA CCTTGGGTCA CATGACAATC TCTCTCCACC   480
TTTTGTCAAT TCCAGAATAC AAAGTAAAAC AGAAAGGGGC TCATACTCAT CTTATGGGAG   540
AGAATCAAAC TTACAGGGTT GCCACCAGCA GAGTCTCCTT GGAGGTGACA TGGATATGGG   600
CAACCCAGGA ACCCTTTCGC CCACCAAACC TGGTTCCCAG TACTATCAGT ATTCTAGCAA   660
TAATCCCCGA AGGAGGCCTC TTCACAGTAG TGCCATGGAG GTACAGACAA AGAAAGTTCG   720
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AAAAGTTCCT CCAGGTTTGC CATCTTCAGT CTATGCTCCA TCAGCAAGCA CTGCCGACTA   780
CAATAGGGAC TCGCCAGGCT ATCCTTCCTC CAAACCAGCA ACCAGCACTT TCCCTAGCTC   840
CTTCTTCATG CAAGATGGCC ATCACAGCAG TGACCCTTGG AGCTCCTCCA GTGGGATGAA   900
TCAGCCTGGC TATGCAGGAA TGTTGGGCAA CTCTTCTCAT ATTCCACAGT CCAGCAGCTA   960
CTGTAGCCTG CATCCACATG AACGTTTGAG CTATCCATCA CACTCCTCAG CAGACATCAA  1020
TTCCAGTCTT CCTCCGATGT CCACTTTCCA TCGTAGTGGT ACAAACCATT ACAGCACCTC  1080
TTCCTGTACG CCTCCTGCCA ACGGGACAGA CAGTATAATG GCAAATAGAG GAAGCGGGGC  1140
AGCCGGCAGC TCCCAGACTG GAGATGCTCT GGGGAAAGCA CTTGCTTCGA TCTATTCTCC  1200
AGATCACACT AACAACAGCT TTTCATCAAA CCCTTCAACT CCTGTTGGCT CTCCTCCATC  1260
TCTCTCAGCA GGCACAGCTG TTTGGTCTAG AAATGGAGGA CAGGCCTCAT CGTCTCCTAA  1320
TTATGAAGGA CCCTTACACT CTTTGCAAAG CCGAATTGAA GATCGTTTAG AAAGACTGGA  1380
TGATGCTATT CATGTTCTCC GGAACCATGC AGTGGGCCCA TCCACAGCTA TGCCTGGTGG  1440
TCATGGGGAC ATGCATGGAA TCATTGGACC TTCTCATAAT GGAGCCATGG GTGGTCTGGG  1500
CTCAGGGTAT GGAACCGGCC TTCTTTCAGC CAACAGACAT TCACTCATGG TGGGGACCCA  1560
TCGTGAAGAT GGCGTGGCCC TGAGAGGCAG CCATTCTCTT CTGCCAAACC AGGTTCCGGT  1620
TCCACAGCTT CCTGTCCAGT CTGCGACTTC CCCTGACCTG AACCCACCCC AGGACCCTTA  1680
CAGAGGCATG CCACCAGGAC TACAGGGGCA GAGTGTCTCC TCTGGCAGCT CTGAGATCAA  1740
ATCCGATGAC GAGGGTGATG AGAACCTGCA AGACACGAAA TCTTCGGAGG ACAAGAAATT  1800
AGATGACGAC AAGAAGGATA TCAAATCAAT TACTAGCAAT AATGACGATG AGGACCTGAC  1860
ACCAGAGCAG AAGGCAGAGC GTGAGAAGGA GCGGAGGATG GCCAACAATG CCCGAGAGCG  1920
TCTGCGGGTC CGTGACATCA ACGAGGCTTT CAAAGAGCTC GGCCGCATGG TGCAGCTCCA  1980
CCTCAAGAGT GACAAGCCCC AGACCAAGCT CCTGATCCTC CACCAGGCGG TGGCCGTCAT  2040
CCTCAGTCTG GAGCAGCAAG TCCGAGAAAG GAATCTGAAT CCGAAAGCTG CGTGTCTGAA  2100
AAGAAGGGAG GAAGAGAAGG TGTCCTCGGA GCCTCCCCCT CTCTCCTTGG CCGGCCCACA  2160
CCCTGGAATG GGAGACGCAT CGAATCACAT GGGACAGATG TAAAAGGGTC CAAGTTGCCA  2220
CATTGCTTCA TTAAAACAAG AGACCACTTC CTTAACAGCT GTATTATCTT AAACCCACAT  2280
AAACACTTCT CCTTAACCCC CATTTTTGTA ATATAAGACA AGTCTGAGTA GTTATGAATC  2340
GCAGACGCAA GAGGTTTCAG CATTCCCAAT TATCAAAAAA CAGAAAAACA AAAAAAAGAA  2400
AGAAAAAAGT GCAACTTGAG GGACGACTTT CTTTAACATA TCATTCAGAA TGTGCAAAGC  2460
AGTATGTACA GGCTGAGACA CAGCCCAGAG ACTGAACGGC
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AAE4 DNA sequence
Gene name: phosphatidylcholine 2-acylhydrolase
Unigene number: Hs.211587
Probeset Accession #: M68874
Nucleic Acid Accession #: M68874
Coding sequence: 139-2388 (predicted start/stop codons underlined)

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CAGTATTCCC ACAAGTTTAC GGTAGTGGTG TTACGTGCCA CCAAAGTGAC AAAGGGGGCC   240
TTTGGTGACA TGCTTGATAC TCCAGATCCC TATGTGGAAC TTTTTATCTC TACAACCCCT   300
GACAGCAGGA AGAGAACAAG ACATTTCAAT AATGACATAA ACCCTGTGTG GAATGAGACC   360
TTTGAATTTA TTTTGGATCC TAATCAGGAA AATGTTTTGG AGATTACGTT AATGGATGCC   420
AATTATGTCA TGGATGAAAC TCTAGGGACA GCAACATTTA CTGTATCTTC TATGAAGGTG   480
GGAGAAAAGA AAGAAGTTCC TTTTATTTTC AACCAAGTCA CTGAAATGGT TCTAGAAATG   540
TCTCTTGAAG TTTGCTCATG CCCAGACCTA CGATTTAGTA TGGCTCTGTG TGATCAGGAG   600
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TCAACCTTGT ATTCTCACCC TGATTTTCCA GAGAAAGGGC CAGAGGAGAT TAATGAAGAA   900
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AGTGCCTTTT CCATATTGTT CAACAGAGTT TTGGGCGTTT CTGGTTCACA AAGCAGAGGC  1380
TCCACAATGG AGGAAGAATT AGAAAATATT ACCACAAAGC ATATTGTGAG TAATGATAGC  1440
TCGGACAGTG ATGATGAATC ACACGAACCC AAAGGCACTG AAAATGAAGA TGCTGGAAGT  1500
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GATTCAGCTT TATTCAATAC CAGAGAAGGA CGTGCTGGGA AGGTACACAA CTTCATGCTG  1620
GGCTTGAATC TCAATACATC TTATCCACTG TCTCCTTTGA GTGACTTTGC CACACAGGAC  1680
TCCTTTGATG ATGATGAACT GGATGCAGCT GTAGCAGATC CTGATGAATT TGAGCGAATA  1740
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TATGAGCCTC TGGATGTCAA AAGTAAAAAG ATTCATGTAG TGGACAGTGG GCTCACATTT 1800
AACCTGCCGT ATCCCTTGAT ACTGAGACCT CAGAGAGGGG TTGATCTCAT AATCTCCTTT 1860
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AAGTGGGCTA AAATGAACAA GCTCCCCTTT CCAAAGATTG ATCCTTATGT GTTTGATCGG 1980
GAAGGGCTGA AGGAGTGCTA TGTCTTTAAA CCCAAGAATC CTGATATGGA GAAAGATTGC 2040
CCAACCATCA TCCACTTTGT TCTGGCCAAC ATCAACTTCA GAAAGTACAA GGCTCCAGGT 2100
GTTCCAAGGG AAACTGAGGA AGAGAAAGAA ATCGCTGACT TTGATATTTT TGATGACCCA 2160
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GATCTTATGC ACTTCAATAC TCTGAACAAC ATTGATGTGA TAAAAGAAGC CATGGTTGAA 2280
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AAATGGCAGC AGTTTCTGAT GCTGAGGCAG TTTGCAATCC CATGACAACT GGATTTAAAA 2460
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GGATATACTT AGCTACATTT TCAGTCAGTA TGAACTTCCT GATACAAATG TAGGGATATA 2640
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ATTCACTGAC TAGATTTATT CATACCATGA GACAACACTA TTTTTATTTA TATATGCATA 2820
TATATACATA CATGAAATAA ATACATCAAT ATAAAAATAA AAAAAAACGG AATTC

ACA1 DNA sequence
Gene name: tissue factor pathway inhibitor 2 TFPI2, placental protein 5 (PP5)
Unigene number: Hs.78045
Probeset Accession #: D29992
Nucleic Acid Accession #: D29992.1
Coding sequence: 57-764 (predicted start/stop codons underlined)

GCCGCCAGCG GCTTTCTCGG ACGCCTTGCC CAGCGGGCCG CCCGACCCCC TGCACCATGG 60
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ACGGACCCTG CCGGGCCCTA CTTCTCCGTT ACTACTACGA CAGGTACACG CAGAGCTGCC 240
GCCAGTTCCT GTACGGGGGC TGCGAGGGCA ACGCCAACAA TTTCTACACC TGGGAGGCTT 300
GCGACGATGC TTGCTGGAGG ATAGAAAAAG TTCCCAAAGT TTGCCGGCTG CAAGTGAGTG 360
TGGACGACCA GTGTGAGGGG TCCACAGAAA AGTATTTCTT TAATCTAAGT TCCATGACAT 420
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GCTTTGCCAG TAGAATCCGG AAAATTCGGA AGAAGCAATT TTAAACATTC TTAATATGTC 780
ATCTTGTTTG TCTTTATGGC TTATTTGCCT TTATGGTTGT ATCTGAAGAA TAATATGACA 840
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TTCAAAAATT TGGATTTTTT TATATATAAC TAGCTGCTAT TCAAATGTGA GTCTACCATT 960
TTTAATTTAT GGTTCAACTG TTTGTGAGAC GAATTCTTGC AATGCATAAG ATATAAAAGC 1020
AAATATGACT CACTCATTTC TTGGGGTCGT ATTCCTGATT TCAGAAGAGG ATCATAACTG 1080
AAACAACATA AGACAATATA ATCATGTGCT TTTAACATAT TTGAGAATAA AAAGGACTAG 1140
CC

ACB8 DNA sequence
Gene name: myosin X
Unigene number: Hs.61638
Probeset Accession #: N77151
Nucleic Acid Accession #: NM_012334
Coding sequence: 223-6399 (predicted start/stop codons underlined)

GAGACAAAGG CTGCCGTCGG GACGGGCGAG TTAGGGACTT GGGTTTGGGC GAACAAAAGG 60
TGAGAAGGAC AAGAAGGGAC CGGGCGATGG CAGCGGGGGA GCCCCGCGGG CGCGCGTCCT 120
CGGGAGTGGC GCCGTGACAC GCATGGTTTC CCCGACCCG CGGCGGCGCT GACTTCCGCG 180
AGTCGGAGCG GCACTCGGCG AGTCCGGGAC TGCGCTGGAA CAATGGATAA CTTCTTCACC 240
GAGGGAACAC GGGTCTGGCT GAGAGAAAAT GGCCAGCATT TTCCAAGTAC TGTAAATTCC 300
TGTGCAGAAG GCATCGTCGT CTTCCGGACA GACTATGGTC AGGTATTCAC TTACAAGCAG 360
AGCACAATTA CCCACCAGAA GGTGACTGCT ATGCACCCCA CGAACGAGGA GGGCGTGGAT 420
GACATGGCGT CCTTGACAGA GCTCCATGGC GGCTCCATCA TGTATAACTT ATTCCAGCGG 480
TATAAGAGAA ATCAAATATA TACCTACATC GGCTCCATCC TGGCCTCCGT GAACCCCTAC 540
CAGCCCATCG CCGGGCTGTA CGAGCCTGCC ACCATGGAGC AGTACAGCCG GCGCCACCTG 600
GGCGAGCTGC CCCCGCACAT CTTCGCCATC GCCAACGAGT GCTACCGCTG CCTGTGGAAG 660

CGCTACGACA ACCAGTGCAT CCTCATCAGT GGTGAAAGTG GGGCAGGTAA AACCGAAAGC 720
ACTAAATTGA TCCTCAAGTT TCTGTCAGTC ATCAGTCAAC AGTCTTTGGA ATTGTCCTTA 780
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ACC3 DNA sequence
Gene name: calcitonin receptor-like (CALCRL)
Unigene number: Hs.152175
Probeset Accession #: L76380
Nucleic Acid Accession #: NM_005795
Coding sequence: 555-1940 (predicted start/stop codons underlined)

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ACC4 DNA sequence
Gene name: Homo sapiens mRNA; cDNA DKFZp586E1624
Unigene number: Hs.94030
Probeset Accession #: AA452000
Nucleic Acid Accession #: AL110152.1
Coding sequence: no ORF identified, possible frameshifts

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ACC5 DNA sequence
Gene name: Selectin E (endothelial adhesion molecule 1)
Unigene number: Hs.89546
Probeset Accession #: M24736
Nucleic Acid Accession #: NM_000450
Coding sequence: 117-1949 (predicted start/stop codons underlined)

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GCTTTGCATT CCTACAAAGA TGTTTGTCAG ATGTGATATG TAAACATAAT TCTTGTATAT 3120

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TATGGAAGAT TTTAAATTCA CAATAGAAAC TCACCATGTA AAAGAGTCAT CTGGTAGATT  3180
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GCTCTGGAAG AGAGGAATGC CTGTGTGAGC AAGCATTTAT GTTTATTTAT AAGCAGATTT  3300
AACAATTCCA AAGGAATCTC CAGTTTTCAG TTGATCACTG GCAATGAAAA ATTCTCAGTC  3360
AGTAATTGCC AAAGCTGCTC TAGCCTTGAG GAGTGTGAGA ATCAAAACTC TCCTACACTT  3420
CCATTAACTT AGCATGTGTT GAAAAAAAAA GTTTCAGAGA AGTTCTGGCT GAACACTGGC  3480
AACGACAAAG CCAACAGTCA AAACAGAGAT GTGATAAGGA TCAGAACAGC AGAGGTTCTT  3540
TTAAAGGGGC AGAAAAACTC TGGGAAATAA GAGAGAACAA CTACTGTGAT CAGGCTATGT  3600
ATGGAATACA GTGTTATTTT CTTTGAAATT GTTTAAGTGT TGTAAATATT TATGTAAACT  3660
GCATTAGAAA TTAGCTGTGT GAAATACCAG TGTGGTTTGT GTTTGAGTTT TATTGAGAAT  3720
TTTAAATTAT AACTTAAAAT ATTTTATAAT TTTTAAAGTA TATATTTATT TAAGCTTATG  3780
TCAGACCTAT TTGACATAAC ACTATAAAGG TTGACAATAA ATGTGCTTAT GTTT
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ACC8 DNA sequence
Gene name: Chemokine (C-X-C motif), receptor 4 (fusin)
Unigene number: Hs.89414
Probeset Accession #: L06797
Nucleic Acid Accession #: NM_003467
Coding sequence: 89-1147 (predicted start/stop codons underlined)

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CTACACCGAG GAAATGGGCT CAGGGGACTA TGACTCCATG AAGGAACCCT GTTTCCGTGA   180
AGAAAATGCT AATTTCAATA AAATCTTCCT GCCCACCATC TACTCCATCA TCTTCTTAAC   240
TGGCATTGTG GGCAATGGAT TGGTCATCCT GGTCATGGGT TACCAGAAGA AACTGAGAAG   300
CATGACGGAC AAGTACAGGC TGCACCTGTC AGTGGCCGAC CTCCTCTTTG TCATCACGCT   360
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TTGTCTTGTG TTTCTTTAGT TTTTGTGAAG TTTAATTGAC TTATTTATAT AAATTTTTTT  1320
TGTTTCATAT TGATGTGTGT CTAGGCAGGA CCTGTGGCCA AGTTCTTAGT TGCTGTATGT  1380
CTCGTGGTAG GACTGTAGAA AAGGGAACTG AACATTCCAG AGCGTGTAGT GAATCACGTA  1440
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ACF2 DNA sequence
Gene name: Endothelial cell-specific molecule 1
Unigene number: Hs.41716
Probeset Accession #: X89426
Nucleic Acid Accession #: NM_007036
Coding sequence: 56-610 (predicted start/stop codons underlined)

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CTGCAAGAGG ACAGTGCTCG ACGACTGTGG CTGCTGCCGA GTGTGCGCTG CAGGGCGGGG   240
AGAAACTTGC TACCGCACAG TCTCAGGCAT GGATGGCATG AAGTGTGGCC CGGGGCTGAG   300
GTGTCAGCCT TCTAATGGGG AGGATCCTTT TGGTGAAGAG TTTGGTATCT GCAAAGACTG   360
TCCCTACGGC ACCTTCGGGA TGGATTGCAG AGAGACCTGC AACTGCCAGT CAGGCATCTG   420
TGACAGGGGG ACGGGAAAAT GCCTGAAATT CCCCTTCTTC CAATATTCAG TAACCAAGTC   480
TTCCAACAGA TTTGTTTCTC TCACGGAGCA TGACATGGCA TCTGGAGATG GCAATATTGT   540
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GCCTTTGAAT GTAAAGCTGC ATAAGCTGTT AGGTTTTGTT TTAAAAGGAC ATGTTTATTA  1980
TTGTTCAATA AAAAAGAACA AGATAC
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ACF4 DNA sequence
Gene name: P53-responsive gene 2 similar to D.melanogaster peroxidasin(U11052)
Unigene number: Hs.118893
Probeset Accession #: D86983
Nucleic Acid Accession #: D86983
Coding sequence: 1-4491 (predicted stop codon underlined, sequence is open at 5' end)

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ACGCTGGCCG TGGTGGCCCA GAAGCCGGGC GCAGGGTGTC CGAGCCGCTG CCTGTGCTTC    180
CGCACCACCG TGCGCTGCAT GCATCTGCTG CTGGAGGCCG TGCCCGCCGT GGCGCCGCAG    240
ACCTCCATCC TAGATCTTCG CTTTAACAGA ATCAGAGAGA TCCAACCTGG GGCATTCAGG    300
CGGCTGAGGA ACTTGAACAC ATTGCTTCTC AATAATAATC AGATCAAGAG GATACCTAGT    360
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TCAATTGACA GGCAAGCATT TAAGGGACTT GCCTCTCTAG AGCAACTATA CCTGCACTTT    480
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GGAGAGGTGA AGACGCAAGA GGTGACCCTC AGGTACTTCG GGTCTCCAGC TCGACCCACT   1080
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TCGGGAACTC TTAGAATCTC TGGTGTTGCC CTCCACGACC AGGGCCAGTA CGAATGCCAG   1560
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CAGGTGACAG AAAGTGGAAA ATTTCACATC AGCCCTGAAG GATTCTTGAC CATCAATGAC   1800
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TCGGTGAGCA TGGTGCTCAG TGTGAACGTT CCTGACGTCA GTCGAAATGG AGATCCGTTT   1920
GTAGCTACCT CCATCGTGGA AGCGATTGCG ACTGTTGACA GAGCTATAAA CTCAACCCGA   1980
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CCCTGGTTGC GTCCACGTCC TGAACAAGAG CCGCTTCCGG ATGGCTCTTC CCAAGGGAGG 5460
AGGAGCTCAA GTGTCGGGAA CTGTCTAACT TCAGGTTGTG TGAGTGCGTT

ACF5 DNA sequence
Gene name: Mitogen-activated protein kinase kinase kinase kinase 4
Unigene number: Hs.3628
Probeset Accession #: N94067
Nucleic Acid Accession #: NM_004834
Coding sequence: 80-3577 (predicted start/stop codons underlined)

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GAAATACTCT CATCACAGAA ACATTGCAAC ATATTATGGT GCTTTCATCA AAAAGAGCCC 360
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GATGGCTCCT GAGGTCATCG CCTGTGATGA GAACCCAGAT GCCACCTATG ATTACAGAAG 720
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ATGGTACCCG GATCCTCGAA TTCC

ACF8 DNA sequence
Gene name: Phospholipase A2, group IVC (cytosolic, calcium-independent)

Unigene number: Hs.18858
Probeset Accession #: AA054087
Nucleic Acid Accession #: NM_003706
Coding sequence: 310-1935 (predicted start/stop codons underlined)

CACGAGGCAG GGGCCATTTT ACCTCCAGGT TGGCCCTGCT CAGGACCAGG AGGAAACACC 60
TCCAGCCCGC GACCTCCTCC CACAGGGGGA AAAGGAAAGC AGGAGGACCA CAGAAGCTTT 120
GGCACCGAGG ATCCCCGCAG TCTTCACCCG CGGAGATTCC GGCTGAAGGA GCTGTCCAGC 180
GACTACACCG CTAAGCGCAG GGAGCCCAAG CCTCCGCACC GGATTCCGGA GCACAAGCTC 240
CACCGCGCAT GCGCACACGC CCCAGACCCA GGCTCAGGAG GACTGAGAAT TTTCTGACCG 300
CAGTGCACCA TGGGAAGCTC TGAAGTTTCC ATAATTCCTG GGCTCCAGAA AGAAGAAAAG 360
GCGGCCGTGG AGAGACGAAG ACTTCATGTG CTGAAAGCTC TGAAGAAGCT AAGGATTGAG 420
GCTGATGAGG CCCCAGTTGT TGCTGTGCTG GGCTCAGGCG GAGGACTGCG GGCTCACATT 480
GCCTGCCTTG GGGTCCTGAG TGAGATGAAA GAACAGGGCC TGTTGGATGC CGTCACGTAC 540
CTCGCAGGGG TCTCTGGATC CACTTGGGCA ATATCTTCTC TCTACACCAA TGATGGTGAC 600
ATGGAAGCTC TCGAGGCTGA CCTGAAACAT CGATTTACCC GACAGGAGTG GGACTTGGCT 660
AAGAGCCTAC AGAAAACCAT CCAAGCAGCG AGGTCTGAGA ATTACTCTCT GACCGACTTC 720
TGGGCCTACA TGGTTATCTC TAAGCAAACC AGAGAACTGC CGGAGTCTCA TTTGTCCAAT 780
ATGAAGAAGC CCGTGGAAGA AGGGACACTA CCCTACCCAA TATTTGCAGC CATTGACAAT 840
GACCTGCAAC CTTCCTGGCA GGAGGCAAGA GCACCAGAGA CCTGGTTCGA GTTCACCCCT 900
CACCACGCTG GCTTCTCTGC ACTGGGGGCC TTTGTTTCCA TAACCCACTT CGGAAGCAAA 960
TTCAAGAAGG GAAGACTGGT CAGAACTCAC CCTGAGAGAG ACCTGACTTT CCTGAGAGGT 1020
TTATGGGGAA GTGCTCTTGG TAACACTGAA GTCATTAGGG AATACATTTT TGACCAGTTA 1080
AGGAATCTGA CCCTGAAAGG TTTATGGAGA AGGGCTGTTG CTAATGCTAA AAGCATTGGA 1140
CACCTTATTT TTGCCCGATT ACTGAGGCTG CAAGAAAGTT CACAAGGGGA ACATCCTCCC 1200
CCAGAAGATG AAGGCGGTGA GCCTGAACAC ACCTGGCTGA CTGAGATGCT CGAGAATTGG 1260
ACCAGGACCT CCCTGGAAAA GCAGGAGCAG CCCCATGAGG ACCCCGAAAG GAAAGGCTCA 1320
CTCAGTAACT TGATGGATTT TGTGAAGAAA ACAGGCATTT GCGCTTCAAA GTGGGAATGG 1380
GGGACCACTC ACAACTTCCT GTACAAACAC GGTGGCATCC GGGACAAGAT AATGAGCAGC 1440
CGGAAGCACC TCCACCTGGT GGATGCTGGT TTAGCCATCA ACACTCCCTT CCCACTCGTG 1500
CTGCCCCCGA CGCGGGAGGT TCACCTCATC CTCTCCTTCG ACTTCAGTGC CGGAGATCCT 1560
TTCGAGACCA TCCGGGCTAC CACTGACTAC TGCCGCCGCC ACAAGATCCC CTTTCCCCAA 1620
GTAGAAGAGG CTGAGCTGGA TTTGTGGTCC AAGGCCCCCG CCAGCTGCTA CATCCTGAAA 1680
GGAGAAACTG GACCAGTGGT GATACATTTT CCCCTGTTCA ACATAGATGC CTGTGGAGGT 1740
GATATTGAGG CATGGAGTGA CACATACGAC ACATTCAAGC TTGCTGACAC CTACACTCTA 1800
GATGTGGTGG TGCTACTCTT GGCATTAGCC AAGAAGAATG TCAGGGAAAA CAAGAAGAAG 1860
ATCCTTAGAG AGTTGATGAA CGTGGCCGGG CTCTACTACC CGAAGGATAG TGCCCGAAGT 1920
TGCTGCTTGG CATAGATGAG CCTCAGCTTC CAGGGCACTG TGGGCCTGTT GGTCTACTAG 1980
GGCCCTGAAG TCCACCTGGC CTTCCTGTTC TTCACTCCCT TCAGCCACAC GCTTCATGGC 2040
CTTGAGTTCA CCTTGGCTGT CCTAACAGGG CCAATCACCA GTGACCAGCT AGACTGTGAT 2100
TTTGATAGCG TCATTCAGAA GAAGGTGTCC AAGGAGCTGA AGGTGGTGAA ATTTGTCCTG 2160
CAGGTCCCTC GGGAGATCCT GGAGCTGGAG CATGAGTGTC TGACAATCAG AAGCATCATG 2220
TCCAATGTCC AGATGGCCAG AATGAATGTG ATAGTTCAGA CCAATGCCTT CCACTGCTCC 2280
TTTATGACTG CACTTCTAGC CAGTAGCTCT GCACAAGTTA GCTCTGTAGA AGTAAGAACT 2340
TGGGCTTAAA TCATGGGCTA TCTCTCCACA GCCAAGTGGA GCTCTGAGAA TACAACAAGT 2400
GCTCAATAAA TGCTTGCTGA TTGACTGATG AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA 2460
AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAA

ACG1 DNA sequence
Gene name: Carbohydrate (chondroitin 6/keratan) sulfotransferase 1
Unigene number: Hs.104576
Probeset Accession #: AA868063
Nucleic Acid Accession #: NM_003654
Coding sequence: 367-1602 (predicted start/stop codons underlined)

GGGGAGGGCG CGGGAGGCGG AGGATGCCGC CGCGGCTGCT GCCGCCGCCG CCACCCGCGG 60
GTCCCCGGCG ACCCTACTCC AGACCCGAGG ATGGAGCCGG CGCTGGGCGC TGCAGCTGCT 120
CCCGGCGCGT CCCCGACCAG GTAGCTGGTG TCACTTCGGT GTGGTTGGAA GAAGACTTTC 180
TCCCCAGCTG CATTCCCGGA GGCGCCCTTT CGACCTGGAG GCCGGGTCTG CTGGCCACAG 240
GGCTGCCGCA CTGGCTGGGA CTGCCAGCTG GGCCTGGAGA CGCTGGTGGC TGTGGACTCC 300
CCAGCTTGGA GCAGTCCCTC TTTGACCTCA CCCCTTGGAG AAGCAGCCCC ATGAAGGTGC 360
CCAGCCATGC AATGTTCCTG GAAGGCCGTC CTCCTCCTTG CCCTGGCCTC CATTGCCATC 420
CAGTACACGG CCATCCGCAC CTTCACCGCC AAGTCCTTTC ACACCTGCCC CGGGCTGGCA 480
GAGGCCGGGC TGGCCGAGCG ACTGTGCGAG GAGAGCCCCA CCTTCGCCTA CAACCTCTCC 540
CGCAAGACCC ACATCCTCAT CCTGGCCACC ACGCGCAGCG GCTCCTCCTT CGTGGGCCAG 600
CTCTTCAACC AGCACCTGGA CGTCTTCTAC CTGTTTGAGC CCCTCTACCA CGTCCAGAAC 660
ACGCTCATCC CCCGCTTCAC CCAGGGCAAG AGCCCGGCCG ACCGGCGGGT CATGCTAGGC 720

GCCAGCCGCG ACCTCCTGCG GAGCCTCTAC GACTGCGACC TCTACTTCCT GGAGAACTAC 780
ATCAAGCCGC CGCCGGTCAA CCACACCACC GACAGGATCT TCCGCCGCGG GGCCAGCCGG 840
GTCCTCTGCT CCCGGCCTGT GTGCGACCCT CCGGGGCCAG CCGACCTGGT CCTGGAGGAG 900
GGGGACTGTG TGCGCAAGTG CGGGCTACTC AACCTGACCG TGGCGGCCGA GGCGTGCCGC 960
GAGCGCAGCC ACGTGGCCAT CAAGACGGTG CGCGTGCCCG AGGTGAACGA CCTGCGCGCC 1020
CTGGTGGAAG ACCCGCGATT AAACCTCAAG GTCATCCAGC TGGTCCGAGA CCCCCGCGGC 1080
ATTCTGGCTT CGCGCAGCGA GACCTTCCGC GACACGTACC GGCTCTGGCG GCTCTGGTAC 1140
GGCACCGGGA GGAAACCCTA CAACCTGGAC GTGACGCAGC TGACCACGGT GTGCGAGGAC 1200
TTCTCCAACT CCGTGTCCAC CGGCCTCATG CGGCCCCCGT GGCTCAAGGG CAAGTACATG 1260
TTGGTGCGCT ACGAGGACCT GGCTCGGAAC CCTATGAAGA AGACCGAGGA GATCTACGGG 1320
TTCCTGGGCA TCCCGCTGGA CAGCCACGTG GCCCGCTGGA TCCAGAACAA CACGCGGGGC 1380
GACCCCACCC TGGGCAAGCA CAAATACGGC ACCGTGCGAA ACTCGGCGGC CACGGCCGAG 1440
AAGTGGCGCT TCCGCCTCTC CTACGACATC GTGGCCTTTG CCCAGAACGC CTGCCAGCAG 1500
GTGCTGGCCC AGCTGGGCTA CAAGATCGCC GCCTCGGAGG AGGAGCTGAA GAACCCCTCG 1560
GTCAGCCTGG TGGAGGAGCG GGACTTCCGC CCCTTCTCGT GACCCGGGCG GTGCGGGTGG 1620
GGGCGGGAGG CGCAAGGTGT CGGTTTTGAT AAAATGGACC GTTTTTAACT GTTGCCTTAT 1680
TAACCCCTCC CTCTCCCACC TCATCTTCGT GTCCTTCCTG CCCCCAGCTC ACCCCACTCC 1740
CTTCTGCCCC TTTTTTGTCT CTGAAATTTG CACTACGTCT TGGACGGGAA TCACTGGGGC 1800
AGAGGGCGCC TGAAGTAGGG TCCCGCCCCC CCCACCCCAT TCAGACACAT GGATGTTGGG 1860
TCTCTGTGCG GACGGTGACA ATGTTTACAA GCACCACATT TACACATCCA CACACGCACA 1920
CGGGCACTCG CGAGGCGACT TCTCAAGCTT TTGAATGGGT GAGTGGTCGG GTATCTAGTT 1980
TTTGCACTGT CTTACTATTC AAGGTAAGAG GATACAAACA AGAGGACCAC TTGTCTCTAA 2040
TTTATGAATG GTGTCCATCC TTTCCCCATC CCTGCCTCCT GCCCCTGACG CCCATTTCCC 2100
CCCTTAGAGC AGCGAAACTG CCCCCTCCTG CCCGCCCTTG CCTGTCGGTG AGGCAGGTTT 2160
TTACTGTGAG GTGAACGTGG ACCTGTTTCT GTTTCCAGTC TGTGGTGATG CTGTCTGTCT 2220
GTCTGAGTCT CGTGGCCGCC CCTGGACCAG TGATGACTGA TGAATCTTAT GAGCTTCTGA 2280
TTGATCTCGG GGTCCATCTG TGATATTTCT TTGTGCCAAA AAGAAAAAAA AAGAGTGGAT 2340
CAGTTTGCTA AATGAACATT GAAATTGAAA TGCTTTATCT GTGTTTTCTG TAAATAAAAG 2400
AGTGCAATAA TCACC

ACG5 DNA sequence
Gene name: Multimerin
Unigene number: Hs.268107
Probeset Accession #: U27109
Nucleic Acid Accession #: U27109.1
Coding sequence: 72-3758 (predicted start/stop codons underlined)

CTGCTATCAA AAAGGCCATA AGGATTTTGT CCCCAAATTT CACATGAGCT ACCTTGCTTC 60
AAACTACTGA GATGAAGGGG GCAAGATTAT TTGTCCTTCT TTCTAGTTTA TGGAGTGGGG 120
GCATTGGGCT TAACAACAGT AAGCATTCTT GGACTATACC TGAGGATGGG AACTCTCAGA 180
AGACTATGCC TTCTGCTTCA GTTCCTCCAA ATAAAATACA AAGTTTGCAA ATACTGCCAA 240
CCACTCGGGT CATGTCGGCG GAGATAGCTA CAACTCCAGA GGCAAGAACT TCTGAAGACA 300
GTCTTCTTAA ATCAACACTG CCTCCCTCAG AAACAAGTGC ACCTGCTGAG GGTGTGAGAA 360
ATCAAACTCT CACATCCACA GAGAAAGCAG AAGGAGTGGT CAAGTTACAG AATCTTACCC 420
TCCCAACCAA CGCTAGCATC AAGTTCAATC CTGGAGCAGA ATCAGTGGTC CTTTCCAATT 480
CTACACTGAA ATTTCTTCAG AGCTTTGCCA GAAAGTCAAA TGAACAAGCA ACTTCTCTAA 540
ACACAGTTGG AGGCACTGGA GGCATTGGAG GCGTTGGAGG CACTGGAGGC GTGGGAAATC 600
GAGCCCCACG GGAAACATAC CTCAGCCGGG GTGACAGCAG TTCCAGCCAA AGAACTGACT 660
ACCAAAAATC AAATTTCGAA ACAACTAGAG GAAAGAATTG GTGTGCTTAT GTACATACCA 720
GGTTATCTCC CACAGTGACA TTGGACAACC AGGTCACTTA TGTCCCAGGT GGGAAAGGAC 780
CTTGTGGCTG GACCGGTGGA TCCTGTCCTC AGAGATCTCA GAAGATATCC AATCCTGTCT 840
ATAGGATGCA ACATAAAATT GTCACCTCAT TGGATTGGAG GTGCTGTCCT GGATACAGTG 900
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AAAGTCATAC AGCTGTTGGC AGAGGAGTAG CTGAGCAGCA GCAGCAGCAA GGCTGTGGTG 1020
ACCCAGAAGT GATGCAAAAA ATGACTGATC AGGTGAACTA CCAGGCAATG AAACTGACTC 1080
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CCTCCCTAGA AGGAAAAGTC AGCGAAGATA AAAGCAGAGA ATTTCAATCT CTTCTAAAAG 1200
GTCTAAAATC CAAAAGCATT AATGTACTGA TAAGAGACAT AGTAAGAGAA CAATTTAAAA 1260
TTTTTCAAAA TGACTTGCAA GAGACTGTAG CACAGCTCTT CAAGACTGTA TCAAGTCTAT 1320
CAGAGGACCT CGAAAGCACC AGGCAAATAA TTCAAAAAGT TAATGAATCT GTGGTTTCAA 1380
TAGCAGCCCA GCAAAAGTTT GTTTTGGTGC AAGAGAATCG GCCCACTTTG ACTGATATAG 1440
TGGAACTAAG GAATCACATT GTGAATGTAA GGCAAGAAAT GACTCTTACA TGTGAGAAGC 1500
CTATTAAAGA ACTAGAAGTA AAGCAGACTC ATTTAGAAGG TGCTCTAGAA CAGGAACACT 1560
CAAGAAGCAT TCTGTATTAT GAATCCCTCA ATAAAACTCT TTCTAAATTG AAGGAAGTAC 1620
ATGAGCAGCT TTTATCAACT GAACAGGTAT CAGACCAGAA GAATGCTCCA GCTGCTGAGT 1680
CAGTTAGCAA TAATGTCACT GAGTACATGT CTACTTTACA TGAAAATATA AAGAAGCAGA 1740
GTTTGATGAT GCTGCAAATG TTTGAAGATT TGCACATTCA AGAAAGCAAG ATTAACAATC 1800

TCACCGTCTC TTTGGAGATG GAGAAAGAGT CTCTCAGAGG TGAATGTGAA GACATGTTAT 1860
CCAAATGCAG AAATGATTTT AAATTTCAAC TTAAGGACAC AGAAGAGAAT TTACATGTGT 1920
TAAATCAAAC ATTGGCTGAA GTTCTCTTTC CAATGGACAA TAAGATGGAC AAAATGAGTG 1980
AGCAACTAAA TGATTTGACT TATGATATGG AGATCCTTCA ACCCTTGCTT GAGCAGGGAG 2040
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CTCAGTTCCA CCGTCTGAAT GATTCTATTC AGACTTTGGT CAATGACAAT CAGAGATATA 2460
ACTTTGTTTT GCAAGTCGCC AAGACCCTTG CAGGTATTCC CAGAGATGAG AAACTAAATC 2520
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ATTTTGAGAC TCGGTTGCAA GACATTGAGT CTAAAGTTAC CCAGACGCTC ATACCTTATT 2700
ATATTTCAGT TAAAAAAGGC AGTGTAGTTA CAAATGAGAG AGATCAGGCT CTTCAACTGC 2760
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AACTTCTTCA GAAAGGTCTA ACAGAATTTG TGGAACCAAT AATTCAAATA AAAACTCAAG 3000
CTGCCCTATC TAATTCAACT TGTTGTATAG ATCGATCGTT GCCTGGTAGT CTGGCAAATG 3060
TTGTCAAGTC TCAGAAGCAA GTAAAATCAT TGCCAAAGAA AATTAACGCA CTTAAGAAAC 3120
CAACGGTAAA TCTTACCACA GTCCTGATAG GCCGGACTCA AAGAAACACG GACAACATAA 3180
TATATCCTGA GGAGTATTCA AGCTGTAGTC GGCATCCGTG CCAAAATGGG GGCACGTGCA 3240
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CTATCAAGCT TGTGGAAGAA AATGCTTTAG CTCCAGATTT TTCCAAAGGA TCTTACAGAT 3360
ATGCACCCAT GGTGGCATTT TTTGCATCTC ATACGTATGG AATGACTATA CCTGGTCCTA 3420
TCCTGTTTAA TAACTTGGAT GTCAATTATG GAGCTTCATA TACCCCAAGA ACTGGAAAAT 3480
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ATGGGCAGGA AGTCTGGTTA CGACTTGCAA AAGGAACAAT TCCAGCCAAG TTTCCCCCTG 3720
TTACTACATT TAGTGGCTAT TTATTATATC GTACATAAGT TAGTATGAAA AACAGACTAT 3780
CACCTTTATT GAGAAACAGC CAGTGTTTTC ATTTATCTTT GCTTGCACAT CTGCTCTGTT 3840
TTGGTTTTTC TACAGGAAAT GAAAATCAAC TTGTTTTTTT AATATGAGTA AACTTGTATG 3900
TCTATTTTAT AAAATTATTT GAATATTGTT TAATGTCTGA ATATGAAAGA GTTCTTGATC 3960
CTAAAGAAAT TTAGTGGCAC AGAAAACAAA GTGAATTTGT TAGCATAATT ATTCCTATTC 4020
TTATTTCTTC ATTTTAAGTC ATTGCAATGG AAAGTAATAT TATAAAACGG TAATTACAAC 4080
ATATTATCAG TCACAGTTTT CTTTCCAATT AAACACTTAA CTTTTGTTAT TCCCTGTATA 4140
TAAATATATA ACACACATTT TCTAGATTCA CAAATTTAAA TAAATTACTC AAAAAATG

ACC6 DNA sequence
Gene name: Homo sapiens cDNA FLJ11502 fis, clone HEMBA1002102, weakly similar to ANKRYIN
Unigene number: Hs.213194
Probeset Accession #: AA187101
Nucleic Acid Accession #: AK021564
Coding sequence: 1-450 (predicted stop codon underlined, 5'end sequence is open)

GTCGCCGCGC GGCCGCCGGT GAGCCGCATG GAGCCCCGGG CGGCGGACGG CTGCTTCCTG 60
GGCGACGTGG GTTTCTGGGT GGAGCGGACC CCTGTGCACG AGGCAGCCCA GCGGGGTGAG 120
AGCCTGCAGC TGCAACAGCT GATCGAGAGC GGCGCCTGCG TGAACCAGGT CACCGTGGAC 180
TCCATCACGC CCCTGCACGC AGCCAGTCTG CAGGGCCAGG CGCGGTGTGT GCAGCTGCTG 240
CTGGCGGCTG GGGCCCAGGT GGATGCTCGC AACATCGACG GCAGCACCCC GCTCTGCGAT 300
GCCTGCGCCT CGGGCAGCAT CGAGTGTGTG AAGCTCTTGC TGTCCTACGG GGCCAAGGTC 360
AACCCTCCCC TGTACACAGC GTCCCCCCTG CACGAGGCCA GCTTTCCCCG CCTCCTGAGC 420
ACCCTGGCTT CGACGCCCTG GATCAACTGA GCCAGGTGGA ACTCCTGGGG GACATGGATC 480
GCAATGAATT CGACCAGTAT TTGAACACTC CTGGCCACCC AGACTCCGCC ACAGGGGCCA 540
TGGCCCTCAG TGGGCATGTT CCGGTCTCCC AGGTCCACC AACGGGTCCC ACAGAGACCA 600
GCCTCATCTC CGTCCTGGCT GATGCCACGG CCACGTACTA CAACAGCTAC AGTGTGTCAT 660
AGAGCTGGAG GCGCCCCGTC CGGTCAGCCC TCGCGCCCTC TCCTTCTTGT GCCTTGAGTG 720
GCAGAGGAGC CGTCCAGCCA CACCAGCTTT CCTCCCACCG CTCAGGGCAG GGAGGTCTGA 780
ACTGCGGCCC CAGAGCCTTT GGCCTAAGCT GGACTCTCCT TATCCGAGTG CCGCCTCTAT 840
CCCCTTCCCC ACGTTCCAGC CCCTGCAGCC CACATTTTAA GTATATTCCT TCAAGTGAGT 900
TTTCCTCCAG CCCCTGAGAG TTGCTGTCTC CCAGTGGAAT GTTCACTGAC GTCTTTTCTT 960
GGTAGCCATC ATCGAAACTA ATGGGGGGAC AGACTTGATA GCCAAGGTCC CTTCTGGTCC 1020
AGTTTTCTGA TTTAGGGTTC TCTCAAGATT AATAAAGGAA GATGGGGAAA TTTGACTCAT 1080

TAATGAGCTC GCTAACCTAC GATCTGGTGA TAATTTTGTG TGCACAGCCC AAGGACCACG 1140
AGGCTTTCTG CACTTTCTGC ACCCCCTTCC AAAGTGACCA CAAAATTTCA AAGGGACTCA 1200
TACAATTTGA GAAAAAACAG TCAACCTGAT TTGAGAAATT AACCAGTATG GCTAACTATA 1260
TCACAGAAAA TGGGATTGAG TTAAAACTAT TTTATTTTAA ATATACATTT TAAAGCAGTT 1320
CTTTTTTTTT TGTTAATTTG TTTATTATAC ACACACTTCA AGAGAATATG CACAGTCTAG 1380
GCCGGGCACG GTGGCTCACG CCTGTAATCC CAGCACTTTG GGAGGCCGAG GCATGTGGAT 1440
CACCTGAGGT CAGGAGTTTG AGACCAGCCT AGACAACATG GTGAAACCTT GTCTCTATGA 1500
AAAATACAAA ATTTGCTGGG AGTGGTGGTG CATGCCTGTA ATCCCAGCTA CTTGGAAGGC 1560
TGAGGCAGGA GAATGTCTTG AACCTAGGAG GTGGAGGTTG CAGTGAGCTG AGATTGCACC 1620
ATTGCACTCC AGCCTGTGCA ACAAGAGTGA AACTCCATTT CAAG

ACC7 DNA sequence
Gene name: Human RAL A gene
Unigene number: Hs.6906
Probeset Accession #: AA083572
Nucleic Acid Accession #: contig of X15014.1 and AK026850
Coding sequence: 1-621 (predicted start/stop codons underlined)

ATGGCTGCAA ATAAGCCCAA GGGTCAGAAT TCTTTGGCTT TACACAAAGT CATCATGGTG 60
GGCAGTGGTG GCGTGGGCAA GTCAGCTCTG ACTCTACAGT TCATGTACGA TGAGTTTGTG 120
GAGGACTATG AGCCTACCAA AGCAGACAGC TATCGGAAGA AGGTAGTGCT AGATGGGGAG 180
GAAGTCCAGA TCGATATCTT AGATACAGCT GGGCAGGAGG ACTACGCTGC AATTAGAGAC 240
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CGAGCTAATG TTGACAAGGT ATTTTTTGAT TTAATGAGAG AAATTCGAGC GAGAAAGATG 540
GAAGACAGCA AAGAAAAGAA TGGAAAAAAG AAGAGGAAAA GTTTAGCCAA GAGAATCAGA 600
GAAAGATGCT GCATTTTATA ATCAAAGCCC AAACTCCTTT CTTATCTTGA CCATACTAAT 660
AAATATAATT TATAAGCATT GCCATTGAAG GCTTAATTGA CTGAAATTAC TTTAACATTT 720
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CTACATTTAT CATGGTCCTG AATGTAGCGT GTAAGCTTGT GTTTCTTGGG CAGTCTTTCT 900
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AAATGACAAT TGTGAACATG ATAGTTAAAC TACCACTTTT TTTAACCATT ATTATGCAAA 1080
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GAATTTTTTG AATATGCCTT AATTTAGAAA CTGAAAAATA TCCGGTTATA TCATTCTGGG 1260
TGTGTTCTTA CTGACACCAG GGGTCCGCTG CCCCATGTGT CCTGGTGAGA AAATATATGC 1320
CTGGCACAGC TTTTGTATAG AAAATTCTTG AGAAGTAACT GTCCGCTAGA AGTCTGTCCA 1380
AATTTAAAAT GTGTGCCATA TTCTGGTTCT TGAAAATAAG ATTCCAGAGC TCTTTGATCG 1440
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TTCTGGTCCC TGGAAATCCC TTTCTGCTAG TGGTGAGCAT GTAAGTGTTA AGTTTTTAAT 1620
CTGGGAGCAG GGCATAGGAA GAAAATGTCA GTAGTGCTAA TGCATTTTGC ACTAGAACGC 1680
TTCGGGAAAA TATTCATGCT TGCCATCTGT TCATTTCTAA ATTTATATTC ATAAAGTTAC 1740
AGTTTGATAC AGGAATTATT AGGAGTAATT CTTTTCTGTT TCTGTTTATA ATGAAGAACA 1800
CTGTAGCTAC ATTTTCAGAA GTTAACATCA AGCCATCAAA CCTGGGTATA GTGCAGAAGA 1860
CGTGGCACAC ACTGACCACA CATTAGGCTG TGTCACCATT GTGTGGTGTA CCTGCTGGAA 1920
GAATTCTAGC ATGCTACTTG GGGACATAAT TTCAGTGGGA AATATGCCAC TGACCGATTT 1980
TTTTTTTTTT CCTCTTTGCA GTGGGGCTAG GACAGTTGAT TCAACAAAGT ATTTTTTTCT 2040
TTTTTCTCAG TCCTAATTTG GACAGGTCAA AGATGTGTTC AGGCATTCCA GGTAACAGGT 2100
GTGTATGTAA AGTTAAAAAT AGGCTTTTTA GGAACTCACT CTTTAGATAT TTACATCCAG 2160
CTTCTCATGT TAAATATTTG TCCTTAAAGG GTTTGAGATG TACATCTTTC ATTTCGTATT 2220
TCTCATAGGC TATGCCATGT GCGGAATTCA AGTTACCAAT GTAACACTGG CCAGCGGGCC 2280
CAGCAATCTC CATGTGTACT TATTACAGTC TTATTTAACC AGGGGTCCTA ACCACTAACA 2340
TTGTGACTTT GCTTTGAGAC CTTTCCTCTC CTGGGTACTG AGGTGCTATG AAGCCAACTG 2400
ACAAAGATGC ATCACGTGTC TTAGGCTGAT GCCACTACCC GATTTGTTTA TTTGCATTTT 2460
GAGCCATTTA AAGACCAATA AACTTCCTTT TTTAAAAAAA AAAAAAAAAA AAAAAAAAAA 2520
A

ACC9 DNA sequence
Gene name: KIAA0955 protein
Unigene number: Hs.10031
Probeset Accession #: AA027168

Nucleic Acid Accession #: AB023172
Coding sequence: 314-1609 (predicted start/stop codons underlined)

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CTGGTTCTCA ACTTCTTTTG AAATAATGTT CATAGAGAAG GAGGGCTGTC TGAGATTCGA     60
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TTTTTCCAAG AAGATGATGA GACAGAGGCA GAGCCATTAT TGTTCCGTGC TGTTCCTGAG    360
TGTCAACTAT CTGGGGGGGA CATTCCCAGG AGACATTTGC TCAGAAGAGA ATCAAATAGT    420
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AAGGGATGAG GTCACAGTGA CGATTGCGTT TGGTTCCTGG AGTCAGCACC TGGCCCTGGA    660
CCTGCAGCAC CATGAACAGT GGCTGGTGGG CGGCCCCTTG TTTGATGTCA CTGCAGAGCC    720
AGAGGAGGCT GTCGCCGAAA TCCACCTCCC CCACTTCATC TCCCTCCAAG GTGAGGTGGA    780
CGTCTCCTGG TTTCTCGTTG CCCATTTTAA GAATGAAGGG ATGGTCCTGG AGCATCCAGC    840
CCGGGTGGAG CCTTTCTATG CTGTCCTGGA AAGCCCCAGC TTCTCTCTGA TGGGCATCCT    900
GCTGCGGATC GCCAGTGGGA CTCGCCTCTC CATCCCCATC ACTTCCAACA CATTGATCTA    960
TTATCACCCC CACCCCGAAG ATATTAAGTT CCACTTGTAC CTTGTCCCCA GCGACGCCTT   1020
GCTAACAAAG GCGATAGATG ATGAGGAAGA TCGCTTCCAT GGTGTGCGCC TGCAGACTTC   1080
GCCCCCAATG GAACCCCTGA ACTTTGGTTC CAGTTATATT GTGTCTAATT CTGCTAACCT   1140
GAAAGTAATG CCCAAGGAGT TGAAATTGTC CTACAGGAGC CCTGGAGAAA TTCAGCACTT   1200
CTCAAAATTC TATGCTGGGC AGATGAAGGA ACCCATTCAA CTTGAGATTA CTGAAAAAAG   1260
ACATGGGACT TTGGTGTGGG ATACTGAGGT GAAGCCAGTG GATCTCCAGC TTGTAGCTGC   1320
ATCAGCCCCT CCTCCTTTCT CAGGTGCAGC CTTTGTGAAG GAGAACCACC GGCAACTCCA   1380
AGCCAGGATG GGGGACCTGA AAGGGGTGCT CGATGATCTC CAGGACAATG AGGTTCTTAC   1440
TGAGAATGAG AAGGAGCTGG TGGAGCAGGA AAAGACACGG CAGAGCAAGA ATGAGGCCTT   1500
GCTGAGCATG GTGGAGAAGA AAGGGGACCT GGCCCTGGAC GTGCTCTTCA GAAGCATTAG   1560
TGAAAGGGAC CCTTACCTCG TGTCCTATCT TAGACAGCAG AATTTGTAAA ATGAGTCAGT   1620
TAGGTAGTCT GGAAGAGAGA ATCCAGCGTT CTCATTGGAA ATGGATAAAC AGAAATGTGA   1680
TCATTGATTT CAGTGTTCAA GACAGAAGAA GACTGGGTAA CATCTATCAC ACAGGCTTTC   1740
AGGACAGACT TGTAACCTGG CATGTACCTA TTGACTGTAT CCTCATGCAT TTTCCTCAAG   1800
AATGTCTGAA GAAGGTAGTA ATATTCCTTT TAAATTTTTT CCAACCATTG CTTGATATAT   1860
CACTATTTTA TCCATTGACA TGATTCTTGA AGACCCAGGA TAAAGGACAT CCGGATAGGT   1920
GTGTTTATGA AGGATGGGGC CTGGAAAGGC AACTTTTCCT GATTAATGTG AAAAATAATT   1980
CCTATGGACA CTCCGTTTGA AGTATCACCT TCTCATAACT AAAAGCAGAA AAGCTAACAA   2040
AAGCTTCTCA GCTGAGGACA CTCAAGGCAT ACATGATGAC AGTCTTTTTT TTTTTGTGTAT   2100
GTTAGGACTT TAACACTTTA TCTATGGCTA CTGTTATTAG AACAATGTAA ATGTATTTGC   2160
TGAAAGAGAG CACAAAAATG GGAGAAAATG CAAACATGAG CAGAAAATAT TTTCCCACTG   2220
GTGTGTAGCC TGCTACAAGG AGTTGTTGGG TTAAATGTTC ATGGTCAACT CCAAGGAATA   2280
CTGAGATGAA ATGTGGTAAA TCAACTCCAC AGAACCACCA AAAAGAAAAT GAGGGTAATT   2340
CAGCTTATTC TGAGACAGAC ATTCCTGGCA ATGTACCATA CAAAAAATAA GCCAACTCTG   2400
ACATTTGGAT TCTACCATAG ACTCTGTCAT TTTGTAGCCA TTTCAGCTGT CTTTTGATTA   2460
ATGTTTTCGT GGCACACATA TTTCCATCCT TTTATGTTTA ATCTGTTTAA AACAAGTTCC   2520
TAGTAGACAC CATCTGGTTG AGTCAGTTTT TTTTATGGTG TATTTTGAAC CCATTCTGAT   2580
AGTCTCTTTT AACTGGAAGA TTTCAATTAC TTACGTTAAT GTAATTATTA ATATGTTAGG   2640
ATTTATCCTC AGTCAGCCAG TTTGTTATGT CTTTTCTATT CTACTGTTAT CACATTTGTA   2700
CCACTTAAAG TGGAATCTAG GCACTTTATC ACCATTTAGA TCCTATTACC TTTTCTCATC   2760
TAGGATATAG TTATCTTCTA CATAATCTTT CTGTATCTTA AAACCCATCA ATAAATTATT   2820
ATATATTTTC TACTTTTAAT CACTCAGAAG ATTTAAAAAA CTCATGAGAA GAGTAATCTG   2880
TTATGTTTTT CCAGATATTT ACCATTTCTG TTGCTCTTCC TTCATTATTT TCCAAATTTC   2940
GTTCTGCAAA TTTCCACTTC TTCTGATAGA CGTTTTTTAG TTCTTTTAGA GTGGTTCTGA   3000
TAGGTACAGA TTCTCTTATT TTTTGCTTCC TCTGAGGACA TCTTTTTCTC ACCTTCATTC   3060
TCAGTGATGT TTTTTGCTTG TAGTATTTTT AGTTGACATT GTTTTCTGTT CAGCAGTTTC   3120
CTTTTAGCTT CCGTATTTCC TGATGAGAAA TCTGCAGTCA TTCAAATTGT TGTTTCCCTG   3180
TATGTAGTGT GTCATTTTTC TGTCAGATTT CAAGGTATTT ATCTTTAGTT TTTAGCCATT   3240
TCATTATGTT GGGGATGAGT TTCCTTGTTT TATTCCCTTT GGAATTTGCT CCAATTCATA   3300
AATTTGCAGT TTTATGTCTT TTACCAAACT TAGAGGTTTT CAGCCTAATT TCTAAAAATA   3360
CTTTTTATTA GCCTGATTTT CATCTTTATA GGAAATAGTT TAAGTGATGA CAAGTTCCAA   3420
TAGCTTATAT GCCCAGAAGG CCTTCAAAAT AAGAATTTTG AAAGAATACA GAAAACAAAC   3480
TTTTATATCC TTCTCATGTC TTCTACTGTA AAATTCATAT GCTTTGCTAC TCTAAACCTA   3540
GTTTGAAATC AACAGTCTTG AGAATAGATG AAAATTTTGA TGAATAGTGG AATTCTTTTA   3600
AATGGAAACC TCTTACATGT GATTTTCCTT GCCATCTAGA AATAAACCAT AGTATTTATG   3660
TTGAATCAAT CAATATTATA TTTTGTTTTT TTCCTCCTCT TCTGAGACTC TTATTGTGGA   3720
AATGTTAGAC TTTTATGTTT TCCTAAATGT CCCTGATATT CTACTTATTT AGAACATCTT   3780
TTCATTTTTT CCATTATTCT GATTGGGTAA TTTTAATTTG TCTATTTTCA AATTTGCTGG   3840
AGTGTTCACC TGTTGTTGTC TGTGTCGTCC CACTGAGTGC ATTCACCACC TTTTAAATTT   3900
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TGGTCACTGT ATGTATCAGT TCTAAAATTT CCATTTTGTT CTCTATATTT TAAATTTCTT 3960
GGCTTATATT CTATTTTCCT GCAAATGTGT CAGCATTTGC TTGTTTGAGC TTTTTTTTTT 4020
TCAAGACAGG GTCTCAACTC TGTTACCCAG GCTGGAGTGC AGTGGTGCGA TCTCAGCTCA 4080
CTGCAACCTC TGCCTCCTGG TTCAAGCGAT TATTGTGCCT CAGCCTCCTG AGTAGCTGGG 4140
ATTACAGGCA TGCACCACCA CAGCCCAGCT AATTTTTTGT ATTTTTAGTA GAGACAGAGT 4200
TTTGCTATGT TGGCCAGGCT GGTTTTGAAC TCCTGGCCTC AAGTGATCCA CCCACCTCAG 4260
CCTCCCAAAG TGCTGGGATT ACAGGCCACT ACACCTGGCA CATTTGAGTA TTTTTTTTTT 4320
TTTTTTTTTT TTGAGATGGA GTCTCGCTCT GTCATCTAGG CTGGAGTGCA GTGGTGTGAT 4380
CTCAGCTCAC TGCAGCCTCT GTCTCCCGGG CTCAAGCGAT TCTCTTGCCT CAGCCTCCTG 4440
AGTAGCTAGG ACTACAGGTG CATGCCAACA CGCCCGGCTA ATTTTTTTAA AAAATATTTT 4500
TAGTAGAGAC AGGGTTTCAC CATTTTGGCC AGGATGGTCT CGATCTCCTG ACCTCATGAT 4560
CCACCCGCCT CGGCCTTCCA AAGTGCTGGG ATTACAGGCA TGAGCCACCG TGCCTGGCCT 4620
CATTTGAGTA TTTTTATAAT GTCTCTTTTA AAGTCTTTGT CAGATAATTC CACTGTACAT 4680
GTTATTCAGT GTTTGGTGTC CACTGAGTTG TCATTTGCCA GACAAGTGGA GATTTTTGCA 4740
GCTCATCCTT GTATTCTCAG TAGTTCCGAT ATGTACCCTC GACATGTGAA TGTTATCTTA 4800
TGAGACTCTG TTTTATTTGT ATCCAACAGA AGATGTTTAT TATTTATTTG GCTTTCTGTG 4860
AACTGAGGTC TTAATATCAG CTCATTTTAA AAGTCTTTGC AGTGGTATTC GGATCTATCC 4920
TGTGTGTGCC TATGAGATTG GGTGCAGTGT ATCCTGTTAG CTCCATTCTC AGGGCGTTTG 4980
AATGTGAATT AGGACCAGCG CAATGAATGC TCAAGTTGGG GTTGGGCGTT AGAATTCATA 5040
AAAGTCTTTA TATGCTCAG

ACF6 DNA sequence
Gene name: Homo sapiens cDNA FLJ10669 fis, clone NT2RP2006275, weakly similar to Microtubule-associated protein 1B [CONTAINS: LIGHT CHAIN LC1]
Unigene number: Hs.66048
Probeset Accession #: AA609717
Nucleic Acid Accession #: AK001531
Coding sequence: 176-2194 (predicted start/stop codons underlined)

CATCTCCCCC AACCTGGGGG TCGTGTTCTT CAACGCCTGC GAGGCCGCGT CGCGGCTGGC 60
GCGCGGCGAG GATGAGGCGG AGCTGGCGCT GAGCCTCCTG GCGCAGCTGG GCATCACGCC 120
TCTGCCACTC AGCCGCGGCC CCGTGCCAGC CAAACCCACC GTGCTCTTCG AGAAGATGGG 180
CGTGGGCCGG CTGGACATGT ATGTGCTGCA CCCGCCCTCC GCCGGCGCCG AGCGCACGCT 240
GGCCTCTGTG TGCGCCCTGC TGGTGTGGCA CCCCGCCGGC CCCGGCGAGA AGGTGGTGCG 300
CGTGCTGTTC CCCGGTTGCA CCCCGCCCGC CTGCCTCCTG GACGGCCTGG TCCGCCTGCA 360
GCACTTGAGG TTCCTGCGAG AGCCCGTGGT GACGCCCCAG GACCTGGAGG GGCCGGGGCG 420
AGCCGAGAGC AAAGAGAGCG TGGGCTCCCG GGACAGCTCG AAGAGAGAGG GCCTCCTGGC 480
CACCCACCCT AGACCTGGCC AGGAGCGCCC TGGGGTGGCC CGCAAGGAGC CAGCACGGGC 540
TGAGGCCCCA CGCAAGACTG AGAAAGAAGC CAAGACCCCC CGGGAGTTGA AGAAAGACCC 600
CAAACCGAGT GTCTCCCGGA CCCAGCCGCG GGAGGTGCGC CGGGCAGCCT CTTCTGTGCC 660
CAACCTCAAG AAGACGAATG CCCAGGCGGC ACCCAAGCCC CGCAAAGCGC CCAGCACGTC 720
CCACTCTGGC TTCCCGCCGG TGGCAAATGG ACCCCGCAGC CCGCCCAGCC TCCGATGTGG 780
AGAAGCCAGC CCCCCCAGTG CAGCCTGCGG CTCTCCGGCC TCCCAGCTGG TGGCCACGCC 840
CAGCCTGGAG CTGGGGCCGA TCCCAGCCGG GGAGGAGAAG GCACTGGAGC TGCCTTTGGC 900
CGCCAGCTCA ATCCCAAGGC CACGCACACC CTCCCCTGAG TCCCACCGGA GCCCCGCAGA 960
GGGCAGCGAG CGGCTGTCGC TGAGCCCACT GCGGGGCGGG GAGGCCGGGC CAGACGCCTC 1020
ACCCACAGTG ACCACACCCA CGGTGACCAC GCCCTCACTA CCCGCAGAGG TGGGCTCCCC 1080
GCACTCGACC GAGGTGGACG AGTCCCTGTC GGTGTCCTTT GAGCAGGTGC TGCCGCCATC 1140
CGCCCCCACC AGTGAGGCTG GGCTGAGCCT CCCGCTGCGT GGCCCCCGGG CGCGGCGCTC 1200
GGCTTCCCCA CACGATGTGG ACCTGTGCCT GGTGTCACCC TGTGAATTTG AGCATCGCAA 1260
GGCGGTGCCA ATGGCACCGG CACCTGCGTC CCCCGGCAGC TCGAATGACA GCAGTGCCCG 1320
GTCACAGGAA CGGGCAGGTG GGCTGGGGGC CGAGGAGACG CCACCCACAT CGGTCAGCGA 1380
GTCCCTGCCC ACCCTGTCTG ACTCGGATCC CGTGCCCCTG GCCCCCGGTG CGGCAGACTC 1440
AGACGAAGAC ACAGAGGGCT TTGGAGTCCC TCGCCACGAC CCTTTGCCTG ACCCCCTCAA 1500
GGTCCCCCCA CCACTGCCTG ACCCATCCAG CATCTGCATG GTGGACCCCG AGATGCTGCC 1560
CCCCAAGACA GCACGGCAAA CGGAGAACGT CAGCCGCACC CGGAAGCCCC TGGCCCGCCC 1620
CAACTCACGC GCTGCCGCCC CCAAAGCCAC TCCAGTGGCT GCTGCCAAAA CCAAGGGGCT 1680
TGCTGGTGGG GACCGTGCCA GCCCACCACT CAGTGCCCGG AGTGAGCCCA GTGAGAAGGG 1740
AGGCCGGGCA CCCCTGTCCA GAAGTCCTC AACCCCCAAG ACTGCCACTC GAGGCCCGTC 1800
GGGGTCAGCC AGCAGCCGGC CCGGGGTGTC AGCCACCCCA CCCAAGTCCC CGGTCTACCT 1860
GGACCTGGCC TACCTGCCCA GCGGGAGCAG CGCCCACCTG GTGGATGAGG AGTTCTTCCA 1920
GCGCGTGCGC GCGCTCTGCT ACGTCATCAG TGGCCAGGAC CAGCGCAAGG AGGAAGGCAT 1980
GCGGGCCGTC CTGGACGCGC TACTGGCCAG CAAGCAGCAT TGGGACCGTG ACCTGCAGGT 2040
GACCCTGATC CCCACTTTCG ACTCGGTGGC CATGCATACG TGGTACGCAG AGACGCACGC 2100
CCGGCACCAG GCGCTGGGCA TCACGGTGTT GGGCAGCAAC GGCATGGTGT CCATGCAGGA 2160
TGACGCCTTC CCGGCCTGCA AGGTGGAGTT CTAGCCCCAT CGCCGACACG CCCCCCACTC 2220
AGCCCAGCCC GCCTGTCCCT AGATTCAGCC ACATCAGAAA TAAACTGTGA CTACACTTG

TABLE 2

AAA4 Protein sequence:
Gene name: CGI-100 protein
Unigene number: Hs.275253
Probeset Accession #: AA089688
Protein Accession #: NP_057124
Signal sequence: predicted 1-23 (first underlined sequence)
Transmembrane Domain: predicted 201-217 (second underlined sequence)
emp24/gp25L/p24 domain: predicted 13-227
Summary: gp25L/emp24/p24 protein family members of the cis-Golgi network bind both COP I and II coatomer. Members of this family are implicated in bringing cargo forward from the ER and binding to coat proteins by their cytoplasmic domains.

MGDKIWLPFP VLLLAALPPV LLPGAAGFTP SLDSDFTFTL PAGQKECFYQ PMPLKASLEI 60
EYQVLDGAGL DIDFHLASPE GKTLVFEQRK SDGVHTVETE VGDYMFCFDN TFSTISEKVI 120
FFELILDNMG EQAQEQEDWK KYITGTDILD MKLEDILESI NSIKSRLSKS GHIQTLLRAF 180
EARDRNIQES NFDRVNFWSM VNLVVMVVVS AIQVYMLKSL FEDKRKSRT

AAA7 Protein sequence:
Gene name: Endothelial differentiation, sphingolipid G-protein-coupled receptor, 1 (EDG1)
Unigene number: Hs.154210
Probeset Accession #: M31210
Protein Accession#: NP_001391
7 Transmembrane Domains: predicted 50-71, 92-110, 122-140, 160-177, 201-222, 251-269, 281-301 (underlined sequences)
Summary: Endothelial differentiation, sphingolipid G-protein-coupled receptor, 1 may regulate the differentiation of endothelial cells. It binds the sphingolipid metabolite, sphingosine-1-phosphate, which may function as a second messenger in cell proliferation and survival.

MGPTSVPLVK AHRSSVSDYV NYDIIVRHYN YTGKLNISAD KENSIKLTSV VFILICCFII 60
LENIFVLLTI WKTKKFHRPM YYFIGNLALS DLLAGVAYTA NLLLSGATTY KLTPAQWFLR 120
EGSMFVALSA SVFSLLAIAI ERYITMLKMK LHNGSNNFRL FLLISACWVI SLILGGLPIM 180
GWNCISALSS CSTVLPLYHK HYILFCTTVF TLLLLSIVIL YCRIYSLVRT RSRRLTFRKN 240
ISKASRSSEN VALLKTVIIV LSVFIACWAP LFILLLLDVG CKVKTCDILF RAEYFLVLAV 300
LNSGTNPIIY TLTNKEMRRA FIRIMSCCKC PSGDSAGKFK RPIIAGMEFS RSKSDNSSHP 360
QKDEGDNPET IMSSGNVNSS S

AAB3 Protein sequence:
Gene name: Solute carrier family 20 (phosphate transporter), member 1, Human leukaemia virus receptor 1 (GLVR1)
Unigene number: Hs.78452
Probeset Accession #: L20859
Protein Accession #: NP_005406
Transmembrane domains: predicted 24-40, 62-78, 164-180, 198-214, 232-248, 513-529, 562-578, 604-620, 655-671
Cellular Localization: Likely a Type IIIa membrane protein (Ncyt Cexo)

MATLITSTTA ATAASGPLVD YLWMLILGFI IAFVLAFSVG ANDVANSFGT AVGSGVVTLK 60
QACILASIFE TVGSVLLGAK VSETIRKGLI DVEMYNSTQG LLMAGSVSAM FGSAVWQLVA 120
SFLKLPISGT HCIVGATIGF SLVAKGQEGV KWSELIKIVM SWFVSPLLSG IMSGILFFLV 180
RAFILHKADP VPNGLRALPV FYACTVGINL FSIMYTGAPL LGFDKLPLWG TILISVGCAV 240
FCALIVWFFV CPRMKRKIER EIKCSPSESP LMEKKNSLKE DHEETKLSVG DIENKHPVSE 300
VGPATVPLQA VVEERTVSFK LGDLEEAPER ERLPSVDLKE ETSIDSTVNG AVQLPNGNLV 360
QFSQAVSNQI NSSGHSQYHT VHKDSGLYKE LLHKLHLAKV GIEMGDSGDK PLRRNNSYTS 420
YTMAICGMPL DSFRAKEGEQ KGEEMEKLTW PNADSKKRIR MLDYTSYCNA VSDLHSASEI 480
DMSVKAAMGL GDRKGSNGSL EEWYDQDKPE VSLLFQFLQI LTACFGSFAH GGNDVSNAIG 540
PLVALYLVYD TGDVSSKVAT PIWLLLYGGV GICVGLWVWG RRVIQTMGKD LTPITPSSGF 600
SIELASALTV VIASNIGLPI STTHCKVGSV VSVGWLRSKK AVDWRLFRNI FMAWFVTVPI 660
SGVISAAIMA IFRYVILRM

AAB4 Protein sequence:

Gene name: Matrix metalloproteinase 10 (stromelysin 2)
Unigene number: Hs.2258
Probeset Accession #: X07820
Protein Accession #: NP_002416
Signal sequence: predicted 1-17 (underlined sequence)
Cellular Localization: predicted secreted

MMHLAFLVLL CLPVCSAYPL SGAAKEEDSN KDLAQQYLEK YYNLEKDVKQ FRRKDSNLIV 60
KKIQGMQKFL GLEVTGKLDT DTLEVMRKPR CGVPDVGHFS SFPGMPKWRK THLTYRIVNY 120
TPDLPRDAVD SAIEKALKVW EEVTPLTFSR LYEGEADIMI SFAVKEHGDF YSFDGPGHSL 180
AHAYPPGPGL YGDIHFDDDE KWTEDASGTN LFLVAAHELG HSLGLFHSAN TEALMYPLYN 240
SFTELAQFRL SQDDVNGIQS LYGPPPASTE EPLVPTKSVP SGSEMPAKCD PALSFDAIST 300
LRGEYLFFKD RYFWRRSHWN PEPEFHLISA FWPSLPSYLD AAYEVNSRDT VFIFKGNEFW 360
AIRGNEVQAG YPRGIHTLGF PPTIRKIDAA VSDKEKKKTY FFAADKYWRF DENSQSMEQG 420
FPRLIADDFP GVEPKVDAVL QAFGFFYFFS GSSQFEFDPN ARMVTHILKS NSWLHC

AAB6 Protein sequence:
Gene name: Podocalyxin-like
Unigene number: Hs.16426
Probeset Accession #: U97519
Protein Accession #: NP_005388
Transmembrane domain: predicted 432-448 (underlined sequence)
Cellular Localization: predicted Type Ia membrane protein (Nexo)

MRCALALSAL LLLLSTPPLL PSSPSPSPSP SPSQNATQTT TDSSNKTAPT PASSVTIMAT 60
DTAQQSTVPT SKANEILASV KATTLGVSSD SPGTTTLAQQ VSGPVNTTVA RGGGSGNPTT 120
TIESPKSTKS ADTTTVATST ATAKPNTTSS QNGAEDTTNS GGKSSHSVTT DLTSTKAEHL 180
TTPHPTSPLS PRQPTLTHPV ATPTSSGHDH LMKISSSSST VAIPGYTFTS PGMTTTLPSS 240
VISQRTQQTS SQMPASSTAP SSQETVQPTS PATALRTPTL PETMSSSPTA ASTTHRYPKT 300
PSPTVAHESN WAKCEDLETQ TQSEKQLVLN LTGNTLCAGG ASDEKLISLI CRAVKATFNP 360
AQDKCGIRLA SVPGSQTVVV KEITIHTKLP AKDVYERLKD KWDELKEAGV SDMKLGDQGP 420
PEEAEDRFSM PLIITIVCMA SFLLLVAALY GCCHQRLSQR KDQQRLTEEL QTVENGYHDN 480
PTLEVMETSS EMQEKKVVSL NGELGDSWIV PLDNLTKDDL DEEEDTHL

AAB8 Protein sequence:
Gene name: EGF-containing fibulin-like extracellular matrix protein 1
Unigene number: Hs.76224
Probeset Accession #: U03877
Protein Accession #: NP_004096 Variant 1
Signal sequence: predicted 1-17 (underlined sequence)
Summary: This gene spans approximately 18 kb of genomic DNA and consists of 12 exons. Two transcripts with distinct 5' UTR have been described; the resulting proteins have distinct N-terminal amino acid sequences. Translation initiation from internal methionine residues was observed with in vitro translation. A signal peptide sequence is predicted for translation initiation sites 1, 2, and 4. The protein isoforms contain 5 or 6 calcium-binding EGF2 domains and 5 or 6 EGF2 domains. Mutations in this gene cause the retinal disease Malattia Leventinese.
Transcript Variant: This variant (1) has a distinct 5' UTR and N-terminal protein sequence as compared to variant 2.

MLKALFLTML TLALVKSQDT EETITYTQCT DGYEWDPVRQ QCKDIDECDI VPDACKGGMK 60
CVNHYGGYLC LPKTAQIIVN NEQPQQETQP AEGTSGATTG VVAASSMATS GVLPGGGFVA 120
SAAAVAGPEM QTGRNNFVIR RNPADPQRIP SNPSHRIQCA AGYEQSEHNV CQDIDECTAG 180
THNCRADQVC INLRGSFACQ CPPGYQKRGE QCVDIDECTI PPYCHQRCVN TPGSFYCQCS 240
PGFQLAANNY TCVDINECDA SNQCAQQCYN ILGSFICQCN QGYELSSDRL NCEDIDECRT 300
SSYLCQYQCV NEPGKFSCMC PQGYQVVRSR TCQDINECET TNECREDEMC WNYHGGFRCY 360
PRNPCQDPYI LTPENRCVCP VSNAMCRELP QSIVYKYMSI RSDRSVPSDI FQIQATTIYA 420
NTINTFRIKS GNENGEFYLR QTSPVSAMLV LVKSLSGPRE HIVDLEMLTV SSIGTFRTSS 480
VLRLTIIVGP FSF

AAB9 Protein sequence:
Gene name: Melanoma adhesion molecule, MUC 18 glycoprotein
Unigene number: Hs.211579
Probeset Accession #: M28882
Protein Accession #: NP_006491

Signal sequence: predicted 1-17 (first underlined sequence)
Transmembrane domain: predicted 558-575 (second underlined sequence)
Cellular localization: predicted Type Ia membrane protein (Nexo)

MGLPRLVCAF LLAACCCCPR VAGVPGEAEQ PAPELVEVEV GSTALLKCGL SQSQGNLSHV 60
DWFSVHKEKR TLIFRVRQGQ GQSEPGEYEQ RLSLQDRGAT LALTQVTPQD ERIFLCQGKR 120
PRSQEYRIQL RVYKAPEEPN IQVNPLGIPV NSKEPEEVAT CVGRNGYPIP QVIWYKNGRP 180
LKEEKNRVHI QSSQTVESSG LYTLQSILKA QLVKEDKDAQ FYCELNYRLP SGNHMKESRE 240
VTVPVFYPTE KVWLEVEPVG MLKEGDRVEI RCLADGNPPP HFSISKQNPS TREAEEETTN 300
DNGVLVLEPA RKEHSGRYEC QAWNLDTMIS LLSEPQELLV NYVSDVRVSP AAPERQEGSS 360
LTLTCEAESS QDLEFQWLRE ETDQVLERGP VLQLHDLKRE AGGGYRCVAS VPSIPGLNRT 420
QLVKLAIFGP PWMAFKERKV WVKENMVLNL SCEASGHPRP TISWNVNGTA SEQDQDPQRV 480
LSTLNVLVTP ELLETGVECT ASNDLGKNTS ILFLELVNLT TLTPDSNTTT GLSTSTASPH 540
TRANSTSTER KLPEPESRGV VIVAVIVCIL VLAVLGAVLY FLYKKGKLPC RRSGKQEITL 600
PPSRKTELVV EVKSDKLPEE MGLLQGSSGD KRAPGDQGEK YIDLRH

AAC1 Protein sequence:
Gene name: Matrix metalloproteinase 1 (interstitial collagenase)
Unigene number: Hs.83169
Probeset Accession #: X54925
Protein Accession #: NP_002412
Signal sequence: predicted 1-19 (underlined sequence)
Cellular localization: predicted secreted protein

MHSFPPLLLL LFWGVVSHSF PATLETQEQD VDLVQKYLEK YYNLKNDGRQ VEKRRNSGPV 60
VEKLKQMQEF FGLKVTGKPD AETLKVMKQP RCGVPDVAQF VLTEGNPRWE QTHLTYRIEN 120
YTPDLPRADV DHAIEKAFQL WSNVTPLTFT KVSEGQADIM ISFVRGDHRD NSPFDGPGGN 180
LAHAFQPGPG IGGDAHFDED ERWTNNFREY NLHRVAAHEL GHSLGLSHST DIGALMYPSY 240
TFSGDVQLAQ DDIDGIQAIY GRSQNPVQPI GPQTPKACDS KLTFDAITTI RGEVMFFKDR 300
FYMRTNPFYP EVELNFISVF WPQLPNGLEA AYEFADRDEV RFFKGNKYWA VQGQNVLHGY 360
PKDIYSSFGF PRTVKHIDAA LSEENTGKTY FFVANKYWRY DEYKRSMDPG YPKMIAHDFP 420
GIGHKVDAVF MKDGFFYFFH GTRQYKFDPK TKRILTLQKA NSWFNCRKN

AAC3 Protein sequence:
Gene name: Branched chain aminotransferase 1, cytosolic
Unigene number: Hs.157205
Probeset Accession #: AA423987
Protein Accession #: NP_005495
Cellular Localization: cytoplasmic
Summary: The lack of the cytosolic enzyme branched-chain amino acid transaminase (BCT) causes cell growth inhibition. There may be at least 2 different clinical disorders due to a defect of branched-chain amino acid transamination: hypervalinemia and hyperleucine-isoleucinemia. Since there are 2 distinct BCATs, mitochondrial and cytosolic, it is possible that one is mutant in each of these 2 conditions.

MDCSNGSAEC TGEGGSKEVV GTFKAKDLIV TPATILKEKP DPNNLVFGTV FTDHMLTVEW 60
SSEFGWEKPH IKPLQNLSLH PGSSALHYAV ELFEGLKAFR GVDNKIRLFQ PNLNMDRMYR 120
SAVRATLPVF DKEELLECIQ QLVKLDQEWV PYSTSASLYI RPAFIGTEPS LGVKKPTKAL 180
LFVLLSPVGP YFSSGTFNPV SLWANPKYVR AWKGGTGDCK MGGNYGSSLF AQCEDVDNGC 240
QQVLWLYGRD HQITEVGTMN LFLYWINEDG EEELATPPLD GIILPGVTRR CILDLAHQWG 300
EFKVSERYLT MDDLTTALEG NRVREMFSSG TACVVCPVSD ILYKGETIHI PTMENGPKLA 360
SRILSKLTDI QYGREESDWT IVLS

ACG4 Protein sequence:
Gene name: Pentaxin-related gene, rapidly induced by IL-1 beta
Unigene number: Hs.2050
Probeset Accession #: M31166
Protein Accession #: NP_002843
Signal sequence: predicted 1-17 (underlined sequence)
Cellular localization: predicted secreted
Summary: TNF-inducible member of hyaluronate binding protein family, related to CD44

MHLLAILFCA LWSAVLAENS DDYDLMYVNL DNEIDNGLHP TEDPTPCDCG QEHSEWDKLF 60

IMLENSQMRE RMLLQATDDV LRGELQRLRE ELGRLAESLA RPCAPGAPAE ARLTSALDEL 120
LQATRDAGRR LARMEGAEAQ RPEEAGRALA AVLEELRQTR ADLHAVQGWA ARSWLPAGCE 180
TAILFPMRSK KIFGSVHPVR PMRLESFSAC IWVKATDVLN KTILFSYGTK RNPYEIQLYL 240
SYQSIVFVVG GEENKLVAEA MVSLGRWTHL CGTWNSEEGL TSLWVNGELA ATTVEMATGH 300
IVPEGGILQI GQEKNGCCVG GGFDETLAFS GRLTGFNIWD SVLSNEEIRE TGGAESCHIR 360
GNIVGWGVTE IQPHGGAQYV S

ACK5 Protein sequence:
Gene name: Von Willebrand factor; Coagulation factor VIII
Unigene number: Hs.110802
Probeset Accession #: M10321
Protein Accession #: NP_000543
Signal peptide: predicted 1-22 (underlined sequence)
Cellular localization: predicted secreted

MIPARFAGVL LALALILPGT LCAEGTRGRS STARCSLFGS DFVNTFDGSM YSFAGYCSYL 60
LAGGCQKRSF SIIGDFQNGK RVSLSVYLGE FFDIHLFVNG TVTQGDQRVS MPYASKGLYL 120
ETEAGYYKLS GEAYGFVARI DGSGNFQVLL SDRYFNKTCG LCGNFNIFAE DDFMTQEGTL 180
TSDPYDFANS WALSSGEQWC ERASPPSSSC NISSGEMQKG LWEQCQLLKS TSVFARCHPL 240
VDPEPFVALC EKTLCECAGG LECACPALLE YARTCAQEGM VLYGWTDHSA CSPVCPAGME 300
YRQCVSPCAR TCQSLHINEM CQERCVDGCS CPEGQLLDEG LCVESTECPC VHSGKRYPPG 360
TSLSRDCNTC ICRNSQWICS NEECPGECLV TGQSHFKSFD NRYFTFSGIC QYLLARDCQD 420
HSFSIVIETV QCADDRDAVC TRSVTVRLPG LHNSLVKLKH GAGVAMDGQD IQLPLLKGDL 480
RIQHTVTASV RLSYGEDLQM DWDGRGRLLV KLSPVYAGKT CGLCGNYNGN QGDDFLTPSG 540
LAEPRVEDFG NAWKLHGDCQ DLQKQHSDPC ALNPRMTRFS EEACAVLTSP TFEACHRAVS 600
PLPYLRNCRY DVCSCSDGRE CLCGALASYA AACAGRGVRV AWREPGRCEL NCPKGQVYLQ 660
CGTPCNLTCR SLSYPDEECN EACLEGCFCP PGLYMDERGD CVPKAQCPCY YDGEIFQPED 720
IFSDHHTMCY CEDGFMHCTM SGVPGSLLPD AVLSSPLSHR SKRSLSCRPP MVKLVCPADN 780
LRAEGLECTK TCQNYDLECM SMGCVSGCLC PPGMVRHENR CVALERCPCF HQGKEYAPGE 840
TVKIGCNTCV CRDRKWNCTD HVCDATCSTI GMAHYLTFDG LKYLFPGECQ YVLVQDYCGS 900
NPGTFRILVG NKGCSHPSVK CKKRVTILVE GGEIELFDGE VNVKRPMKDE THFEVVESGR 960
YIILLLGKAL SVVWDRHLSI SVVLKQTYQE KVCGLCGNFD GIQNNDLTSS NLQVEEDPVD 1020
FGNSWKVSSQ CADTRKVPLD SSPATCHNNI MKQTMVDSSC RILTSDVFQD CNKLVDPEPY 1080
LDVCIYDTCS CESIGDCACF CDTIAAYAHV CAQHGKVVTW RTATLCPQSC EERNLRENGY 1140
ECEWRYNSCA PACQVTCQHP EPLACPVQCV EGCHAHCPPG KILDELLQTC VDPEDCPVCE 1200
VAGRRFASGK KVTLNPSDPE HCQICHCDVV NLTCEACQEP GGLVVPPTDA PVSPTTLYVE 1260
DISEPPLHDF YCSRLLDLVF LLDGSSRLSE AEFEVLKAFV VDMMERLRIS QKWVRVAVVE 1320
YHDGSHAYIG LKDRKRPSEL RRIASQVKYA GSQVASTSEV LKYTLFQIFS KIDRPEASRI 1380
ALLLMASQEP QRMSRNFVRY VQGLKKKKVI VIPVGIGPHA NLKQIRLIEK QAPENKAFVL 1440
SSVDELEQQR DEIVSYLCDL APEAPPPTLP PHMAQVTVGP GLLGVSTLGP KRNSMVLDVA 1500
FVLEGSDKIG EADFNRSKEF MEEVIQRMDV GQDSIHVTVL QYSYMVTVEY PFSEAQSKGD 1560
ILQRVREIRY QGGNRTNTGL ALRYLSDHSF LVSQGDREQA PNLVYMVTGN PASDEIKRLP 1620
GDIQVVPIGV GPNANVQELE RIGWPNAPIL IQDFETLPRE APDLVLQRCC SGEGLQIPTL 1680
SPAPDCSQPL DVILLLDGSS SFPASYFDEM KSFAKAFISK ANIGPRLTQV SVLQYGSITT 1740
IDVPWNVVPE KAHLLSLVDV MQREGGPSQI GDALGFAVRY LTSEMHGARP GASKAVVILV 1800
TDVSVDSVDA AADAARSNRV TVFPIGIGDR YDAAQLRILA GPAGDSNVVK LQRIEDLPTM 1860
VTLGNSFLHK LCSGFVRICM DEDGNEKRPG DVWTLPDQCH TVTCQPDGQT LLKSHRVNCD 1920
RGLRPSCPNS QSPVKVEETC GCRWTCPCVC TGSSTRHIVT FDGQNFKLTG SCSYVLFQNK 1980
EQDLEVILHN GACSPGARQG CMKSIEVKHS ALSVELHSDM EVTVNGRLVS VPYVGGNMEV 2040
NVYGAIMHEV RFNHLGHIFT FTPQNNEFQL QLSPKTFASK TYGLCGICDE NGANDFMLRD 2100
GTVTTDWKTL VQEWTVQRPG QTCQPILEEQ CLVPDSSHCQ VLLLPLFAEC HKVLAPATFY 2160
AICQQDSCHQ EQVCEVIASY AHLCRTNGVC VDWRTPDFCA MSCPPSLVYN HCEHGCPRHC 2220
DGNVSSCGDH PSEGCFCPPD KVMLEGSCVP EEACTQCIGE DGVQHQFLEA WVPDHQPCQI 2280
CTCLSGRKVN CTTQPCPTAK APTCGLCEVA RLRQNADQCC PEYECVCDPV SCDLPPVPHC 2340
ERGLQPTLTN PGECRPNFTC ACRKEECKRV SPPSCPPHRL PTLRKTQCCD EYECACNCVN 2400
STVSCPLGYL ASTATNDCGC TTTTCLPDKV CVHRSTIYPV GQFWEEGCDV CTCTDMEDAV 2460
MGLRVAQCSQ KPCEDSCRSG FTYVLHEGEC CGRCLPSACE VVTGSPRGDS QSSWKSVGSQ 2520
WASPENPCLI NECVRVKEEV FIQQRNVSCP QLEVPVCPSG FQLSCKTSAC CPSCRCERME 2580
ACMLNGTVIG PGKTVMIDVC TTCRCMVQVG VISGFKLECR KTTCNPCPLG YKEENNTGEC 2640
CGRCLPTACT IQLRGGQIMT LKRDETLQDG CDTHFCKVNE RGEYFWEKRV TGCPPFDEHK 2700
CLAEGGKIMK IPGTCCDTCE EPECNDITAR LQYVKVGSCK SEVEVDIHYC QGKCASKAMY 2760
SIDINDVQDQ CSCCSPTRTE PMQVALHCTN GSVVYHEVLN AMECKCSPRK CSK

AAC7 protein sequence:
Gene name: KIAA1294 protein
Probeset Accession #: AA432248

Protein Accession #: BAA92532
Cellular localization: predicted nuclear protein
PFAM prediction: 22-153 Band 41 domain (underlined seq). A number of cytoskeletal-associated proteins that associate with various proteins at the interface between the plasma membrane and the cytoskeleton contain a conserved N-terminal domain of about 150 amino-acid residues.

```
MAVQLVPDSA LGLLMMTEGR RCQVHLLDDR KLELLVQPKL LAKELLDLVA SHFNLKEKEY     60
FGIAFTDETG HLNWLQLDRR VLEHDFPKKS GPVVLYFCVR FYIESISYLK DNATIELFFL    120
NAKSCIYKEL IDVDSEVVFE LASYILQEAK GDFSSNEVVR SDLKKLPALP TQALKEHPSL    180
AYCEDRVIEH YKKLNGQTRG QAIVNYMSIV ESLPTYGVHY YAVKDKQGIP WWLGLSYKGI    240
FQYDYHDKVK PRKIFQWRQL ENLYFREKKF SVEVHDPRRA SVTRRTFGHS GIAVHTWYAC    300
PALIKSIWAM AISQHQFYLD RKQSKSKIHA ARSLSEIAID LTETGTLKTS KLANMGSKGK    360
IISGSSGSLL SSGSQESDSS QSAKKDMLAA LKSRQEALEE TLRQRLEELK KLCLREAELT    420
GKLPVEYPLD PGEEPPIVRR RIGTAFKLDE QKILPKGEEA ELERLEREFA IQSQITEAAR    480
RLASDPNVSK KLKKQRKTSY LNALKKLQEI ENAINENRIK SGKKPTQRAS LIIDDGNIAS    540
EDSSLSDALV LEDEDSQVTS TISPLHSPHK GLPPRPPSHN RPPPPQSLEG LRQMHYHRND    600
YDKSPIKPKM WSESSLDEPY EKVKKRSSHS HSSSHKRFPS TGSCAEAGGG SNSLQNSPIR    660
GLPHWNSQSS MPSTPDLRVR SPHYVHSTRS VDISPTRLHS LALHFRHRSS SLESQGKLLG    720
SENDTGSPDF YTPRTRSSNG SDPMDDCSSC TSHSSSEHYY PAQMNANYST LAEDSPSKAR    780
QRQRQRQRAA GALGSASSGS MPNLAARGGA GGAGGAGGGV YLHSQSQPSS QYRIKEYPLY    840
IEGGATPVVV RSLESDQECH YSVKAQFKTS NSYTAGGLFK ESWRGGGGDE GDTGRLTPSR    900
SQILRTPSLG REGAHDKGAG RAAVSDELRQ WYQRSTASHK EHSRLSHTSS TSSDSGSQYS    960
TSSQSTFVAH SRVTRMPQMC KATSAALPQS QRSSTPSSEI GATPPSSPHH ILTWQTGEAT   1020
ENSPILDGSE SPPHQSTDE
```

ACG8 Protein sequence:
Gene name: ubiquitin E3 ligase SMURF2
Unigene number: Hs.21806 (3'UTR only)
Probeset Accession #: AA398243
Protein Accession #: AF301463_1
Cellular Localization: predicted cytoplasmic
Summary: Smurf2 is a Ubiquitin E3 Ligase Mediating Proteasome-dependent Degradation of Smad2 in Transforming Growth Factor-beta Signaling

```
MSNPGGRRNG PVKLRLTVLC AKNLVKKDFF RLPDPFAKVV VDGSGQCHST DTVKNTLDPK     60
WNQHYDLYIG KSDSVTISVW NHKKIHKKQG AGFLGCVRLL SNAINRLKDT GYQRLDLCKL    120
GPNDNDTVRG QIVVSLQSRD RIGTGGQVVD CSRLFDNDLP DGWEERRTAS GRIQYLNHIT    180
RTTQWERPTR PASEYSSPGR PLSCFVDENT PISGTNGATC GQSSDPRLAE RRVRSQRHRN    240
YMSRTHLHTP PDLPEGYEQR TTQQGQVYFL HTQTGVSTWH DPRVPRDLSN INCEELGPLP    300
PGWEIRNTAT GRVYFVDHNN RTTQFTDPRL SANLHLVLNR QNQLKDQQQQ QVVSLCPDDT    360
ECLTVPRYKR DLVQKLKILR QELSQQQPQA GHCRIEVSRE EIFEESYRQV MKMRPKDLWK    420
RLMIKFRGEE GLDYGGVARE WLYLLSHEML NPYYGLFQYS RDDIYTLQIN PDSAVNPEHL    480
SYFHFVGRIM GMAVFHGHYI DGGFTLPFYK QLLGKSITLD DMELVDPDLH NSLVWILEND    540
ITGVLDHTFC VEHNAYGEII QHELKPNGKS IPVNEENKKE YVRLYVNWRF LRGIEAQFLA    600
LQKGFNEVIP QHLLKTFDEK ELELIICGLG KIDVNDWKVN TRLKHCTPDS NIVKWFWKAV    660
EFFDEERRAR LLQFVTGSSR VPLQGFKALQ GAAGPRLFTI HQIDACTNNL PKAHTCFNRI    720
DIPPYESYEK LYEKLLTAIE ETCGFAVE
```

ACH3 Protein sequence:
Gene name: EST
Unigene number: Hs.30089
Probeset Accession #: AA410480
CAT cluster#: cluster 96816_1
Summary: predicted open reading frame

```
PLWTEPPLSC CLPATYPADR GPAEPCSCAG VILGFLLFRG HNSQPTMTQT SPSQGGLGGL     60
SLTTEPVSSN PGYIPSSEAN RPSHLSSTGT PGAGVPSSGR DGGTSRDTFQ TPPNSTTMS     120
LSMREDATIL PSPTSETVLT VAAFGVISFI VILVVVVIIL VGVVSLRFKC RKSKESGDPQ     180
KPGEREEKVG HRREPYPWN
```

ACJ2 Protein sequence:
Gene name: Complement component C1q receptor
Unigene number: Hs.97199
Probeset Accession #: AA487558

Protein Accession #: NP_036204
Signal sequence: 1-17 (first underlined sequence)
Transmemrane domain: 589-605 (second underlined sequence)
Cellular localization: This gene encodes a predicted type I membrane protein.
Summary: This protein acts as a receptor for complement protein C1q, mannose-binding lectin, and pulmonary surfactant protein A. This protein is a functional receptor involved in ligand-mediated enhancement of phagocytosis.

MATSMGLLLL LLLLLTQPGA GTGADTEAVV CVGTACYTAH SGKLSAAEAQ NHCNQNGGNL 60
ATVKSKEEAQ HVQRVLAQLL RREAALTARM SKFWIGLQRE KGKCLDPSLP LKGFSWVGGG 120
EDTPYSNWHK ELRNSCISKR CVSLLLDLSQ PLLPNRLPKW SEGPCGSPGS PGSNIEGFVC 180
KFSFKGMCRP LALGGPGQVT YTTPFQTTSS SLEAVPFASA ANVACGEGDK DETQSHYFLC 240
KEKAPDVFDW GSSGPLCVSP KYGCNFNNGG CHQDCFEGGD GSFLCGCRPG FRLLDDLVTC 300
ASRNPCSSSP CRGGATCVLG PHGKNYTCRC PQGYQLDSSQ LDCVDVDECQ DSPCAQECVN 360
TPGGFRCECW VGYEPGGPGE GACQDVDECA LGRSPCAQGC TNTDGSFHCS CEEGYVLAGE 420
DGTQCQDVDE CVGPGGPLCD SLCFNTQGSF HCGCLPGWVL APNGVSCTMG PVSLGPPSGP 480
PDEEDKGEKE GSTVPRAATA SPTRGPEGTP KATPTTSRPS LSSDAPITSA PLKMLAPSGS 540
SGVWREPSIH HATAASGPQE PAGGDSSVAT QNNDGTDGQK LLLFYILGTV VAILLLLALA 600
LGLLVYRKRR AKREEKKEKK PQNAADSYSW VPERAESRAM ENQYSPTPGT DC

ACJ3 Protein sequence:
Gene name: FLT1/vascular endothelial growth factor receptor
Unigene number: Hs.138671
Probeset Accession #: AA047437
Transmembrane domain: predicted 764-780 (underlined sequence)
Cellular Localization: predicted cell surface tyrosine kinase

MVSYWDTGVL LCALLSCLLL TGSSSGSKLK DPELSLKGTQ HIMQAGQTLH LQCRGEAAHK 60
WSLPEMVSKE SERLSITKSA CGRNGKQFCS TLTLNTAQAN HTGFYSCKYL AVPTSKKKET 120
ESAIYIFISD TGRPFVEMYS EIPEIIHMTE GRELVIPCRV TSPNITVTLK KFPLDTLIPD 180
GKRIIWDSRK GFIISNATYK EIGLLTCEAT VNGHLYKTNY LTHRQTNTII DVQISTPRPV 240
KLLRGHTLVL NCTATTPLNT RVQMTWSYPD EKNKRASVRR RIDQSNSHAN IFYSVLTIDK 300
MQNKDKGLYT CRVRSGPSFK SVNTSVHIYD KAFITVKHRK QQVLETVAGK RSYRLSMKVK 360
AFPSPEVVWL KDGLPATEKS ARYLTRGYSL IIKDVTEEDA GNYTILLSIK QSNVFKNLTA 420
TLIVNVKPQI YEKAVSSFPD PALYPLGSRQ ILTCTAYGIP QPTIKWFWHP CNHNHSEARC 480
DFCSNNEESF ILDADSNMGN RIESITQRMA IIEGKNKMAS TLVVADSRIS GIYICIASNK 540
VGTVGRNISF YITDVPNGFH VNLEKMPTEG EDLKLSCTVN KFLYRDVTWI LLRTVNNRTM 600
HYSISKQKMA ITKEHSITLN LTIMNVSLQD SGTYACRARN VYTGEEILQK KEITIRDQEA 660
PYLLRNLSDH TVAISSSTTL DCHANGVPEP QITWFKNNHK IQQEPGIILG PGSSTLFIER 720
VTEEDEGVYH CKATNQKGSV ESSAYLTVQG TSDKSNLELI TLTCTCVAAT LFWLLLTLLI 780
RKMKRSSSEI KTDYLSIIMD PDEVPLDEQC ERLPYDASKW EFARERLKLG KSLGRGAFGK 840
VVQASAFGIK KSPTCRTVAV KMLKEGATAS EYKALMTELK ILTHIGHHLN VVNLLGACTK 900
QGGPLMVIVE YCKYGNLSNY LKSKRDLFFL NKDAALHMEP KKEKMEPGLE QGKKPRLDSV 960
TSSESFASSG FQEDKSLSDV EEEEDSDGFY KEPITMEDLI SYSFQVARGM EFLSSRKCIH 1020
RDLAARNILL SENNVVKICD FGLARDIYKN PDYVRKGDTR LPLKWMAPES IFDKIYSTKS 1080
DVWSYGVLLW EIFSLGGSPY PGVQMDEDFC SRLREGMRMR APEYSTPEIY QIMLDCWHRD 1140
PKERPRFAEL VEKLGDLLQA NVQQDGKDYI PINAILTGNS GFTYSTPAFS EDFFKESISA 1200
PKFNSGSSDD VRYVNAFKFM SLERIKTFEE LLPNATSMFD DYQGDSSTLL ASPMLKRFTW 1260
TDSKPKASLK IDLRVTSKSK ESGLSDVSRP SFCHSSCGHV SEGKRRFTYD HAELERKIAC 1320
CSPPPDYNSV VLYSTPPI

ACJ9 Protein sequence:
Gene name: Purine nucleoside phosphorylase
Unigene number: Hs.75514
Probeset Accession #: K02574
Protein Accession #: CAA25320
Cellular Localization: predicted cytoplasmic
Summary: likely to catalyze the reversible phosphorolytic cleavage of purine ribonucleosides and 2'-deoxyribonucleosides

MENGYTYEDY KNTAEWLLSH TKHRPQVAII CGSGLGGLTD KLTQAQIFDY SEIPNFPRST 60
VPGHAGRLVF GFLNGRACVM MQGRFHMYEG YPLWKVTFPV RVFHLLGVDT LVVTNAAGGL 120
NPKFEVGDIM LIRDHINLPG FSGQNPLRGP NDERFGDRFP AMSDAYDRTM RQRALSTWKQ 180
MGEQRELQEG TYVMVAGPSF ETVAECRVLQ KLGADAVGMS TVPEVIVARH CGLRVFGFSL 240
ITNKVIMDYE SLEKANHEEV LAAGKQAAQK LEQFVSILMA SIPLPDKAS

ACK4 Protein sequence

Gene name: EST

Probeset Accession #: R68763

Predicted amino acid seq: FGENESH exon prediction on BAC clone AC009414

Predicted nuclear target motifs: from 25 (4) RRRP (underlined); 176 (5) RRRR (underlined); 177 (5) RRRR (underlined; 239 (5) KRKK (underlined); 399 (4) PPRARRT (underlined); 400 (5) PRARRTE (underlined)

Cellular localization: predicted nuclear

MPPEQHHQPN KVSPKLCSAQ PAPRGRRRPG GRGPAAGGRT FANARFVLGE GVAIERGADD 60
TTQPPVAGSV NPEGAAAALV PLAGARVAAA ADALHDAPRA VPGLLALGLV TGQADQRPGA 120
GARQQQQQPQ QRDQEVPAAG QPPVPRHQVH PPAPPPPPPR SRAGSGAGAL PCAGHTRRRR 180
RTSSPRSSPP LSGPPGRASP RGARPPPLLR AAPTPSPRAL APAAASPPPP PPPPGREGEK 240
RKKFPPGSSG STQTSGAAAA VAAALGSSPG RRRLLPLLLR VGRPRSGAAS GPVPASRAAE 300
WARWRSTRSA ASAPRAPLAS LLRRSSGRLF MAGASAARAA PSPILPPPPD LPPTPTRRAP 360
LIGCPPSPAR PAPSASPSPS RAAGPFLPPS HASTSSRSPP PRARRTEPAV PPSCGSGPGA 420
AGALRMGLGR TQRAARVAVS RALAGTVAAA AGLGARRARR LHLRGQIGVR RVAGTPEARG 480
RGDGCSLGRV SPDRTPGKGS KGMEPPHTG

AAA8 Protein sequence:

Gene name: ETL protein, with extended open reading frame

Unigene number: Hs.57958

Probeset Accession #: D58024

Protein Accession #: AAG33021

Transmembrane domains: predicted 454-470, 486-502, 511-527, 528-544, 556-572, 600-616, 642-661, 672-689 (underlined sequences)

Extended sequence: Residues 1-564 were added to the sequence in AAG33021

Cellular Localization: predicted cell surface serpentine receptor

MKTAALTPPR SPPPPPLRPP PMKRLPLLVV FSTLLNCSYT QNCTKTPCLP NAKCEIRNGI 60
EACYCNMGFS GNGVTICEDD NECGNLTQSC GENANCTNTE GSYYCMCVPG FRSSSNQDRF 120
ITNDGTVCIE NVNANCHLDN VCIAANINKT LTKIRSIKEP VALLQEVYRN SVTDLSPTDI 180
ITYIEILAES SSLLGYKNNT ISAKDTLSNS TLTEFVKTVN NFVQRDTFVV WDKLSVNHRR 240
THLTKLMHTV EQATLRISQS FQKTTEFDTN STDIALKVFF FDSYNMKHIH PHMNMDGDYI 300
NIFPKRKAAY DSNGNVAVAF LYYKSIGPLL SSSDNFLLKP QNYDNSEEEE RVISSVISVS 360
MSSNPPTLYE LEKITFTLSH RKVTDRYRSL CAFWNYSPDT MNGSWSSEGC ELTYSNETHT 420
SCRCNHLTHF AILMSSGPSI GIKDYNILTR ITQLGIIISL ICLAICIFTF WFFSEIQSTR 480
TTIHKNLCCS LFLAELVFLV GINTNTNKLX SVSIIAGLLH YFFLAAFAWM CIEGIHLYLI 540
VVGVIYNKGF LHKNFYIFGY LSPAVVVGFS AALGYRYYGT TKVCWLSTET HFIWSFIGPA 600
CLIILVNLLA FGVIIYKVFR HTAGLKPEVS CFENIRSCAR GALALLFLLG TTWIFGVLHV 660
VHASVVTAYL FTVSNAFQGM FIFLFLCVLS RKIQEEYYRL FKNVPCCFGC LR

AAC6 Protein sequence:

Gene name: EST

Unigene number: Hs.134797

Probeset Accession #: AA025351

Protein accession #: BAB14599

Signal sequence: predicted 1-24 (first underlined sequence)

extended sequence: second underlined sequence

MILSLLFSLG GPLGWGLLGA WAQASSTSLS DLQSSRTPGV WKAEAEDTSK DPVGRNWCPY 60
PMSKLVTLLA LCKTEKFLIH SQQPCPQGAP DCQKVKVMYR MAHKPVYQVK QKVLTSLAWR 120
CCPGYTGPNC EHHDSMAIPE PADPGDSHQE PQDGPVSFKP GHLAAVINEV EVQQEQQEHL 180
LGDLQNDVHR VADSLPGLWK ALPGNLTAAV MEANQTGHEF PDRSLEQVLL PHVDTFLQVH 240
FSPIWRSFNQ SLHSLTQAIR NLSLDVEANR QAISRVQDSA VARADFQELG AKFEAKVQEN 300
TQRVGQLRQD VEDRLHAQHF TLHRSISELQ ADVDTKLKRL HKAQEAPGTN GSLVLATPGA 360
GARPEPDSLQ ARLGQLQE.. SELHMTTARR EEELQYTLED MRATLTRHVD EIKELYSESD 420
ETFDQISKVE RQVEELQVAH TALRELRVIL MEKSLIMEEN KEEVERQLLE LNLTLQHLQG 480
GHADLIKYVK DCNCQKLYLD LDVIREGQRD ATRALEETQV SLDERRQLDG SSLQALQNAV 540
DAVSLAVDAH KAEGERARAA TSRLRSQVQA LDDEVGALKA AAAEARHEVR QLHSAFAALL 600
EDALRHEAVL AALFGEEVLE EMSEQTPGPL PLSYEQIRVA LQDAASGLQE QALGWDELAA 660
RVTALEQASE PPRPAEHLEP SHDAGREEAA TTALAGLARE LQSLSNDVKN VGRCCEAEAG 720
AGAASLNASL DGLHNALFAT QRSLEQHQRL FHSLFGNFQG LMEANVSLDL GKLQTMLSRK 780
GKKQQKDLEA PRKRDKKEAE PLVDIRVTGP VPGALGAALW EASPVAFYAS FSEGTAALQT 840
VKFNTTYINI GSSYFPEHGY FRAPERGVYL FAVSVEFGPG PGTGQLVFGG HHRTPVCTTG 900

QGSGSTATVF AMAELQKGER VWFELTQGSI TKRSLSGTAF GGFLMFKT

ACH7 Protein sequence:
Gene name: EST
Unigene number: Hs.3807
Probeset Accession #: AA292694
BAC Accession #: AL161751
FGENESH predicted aa seq: 1-647; based on BAC clone AL161751

```
MGKDFMTKTP KAFATKAKID KWDLIKLKSF CTAKETIIRV NSQPTDWQKT FAIYPSDKGV     60
IARIYKELEQ IYKKKKPTKT LRTHFLSRPK GNCWPLGPRG DSWQLGGPSG ARAEGKGGGT    120
GLGKPAVEGG DRAPDTALRP RAGQIQVGSS SACGASENEA GVRPVPPLAG ALARAGRRRT    180
PHCRPCWLLG LGGLLQPAPR YHEAAGGRGG LHPARWGAQH RACGRRAARC ARAPAGRPRA    240
RRGLQRPAVL GRTGAQAFPL HPGERAFAGF LLAVLRPRRS RKRHAAVGGG APTLLHRAEM    300
RGTPGHRWGR ARSWKEMRCH LRANGYLCKY QFEVLCPAPR PGAASNLSYR APFQLHSAAL    360
DFSPPGTEVS ALCRGQLPIS VTCIADEIGA RWDKLSGDVL CPCPGRYLRA GKCAELPNCL    420
DDLGGFACEC ATGFELGKDG RSCVTSGEGQ PTLGGTGVPT RRPPATATSP VPQRTWPIRV    480
DEKLGETPLV PEQDNSVTSI PEIPRWGSQS TMSTLQMSLQ AESKATITPS GSVISKFNST    540
TSSATPQAFD SSSAVVFIFV STAVVVLVIL TMTVLGLVKL CFHESPSSQP RKESMGPPGL    600
ESDPEPAALG SSSAHCTNNG VKVGDCDLRD RAEGALLAES PLGSSDA
```

AAD4 Protein sequence
Gene name: ERG
Unigene number: Hs.45514
Probeset Accession #: R32894
Protein Accession #: AAA52398
Signal sequence: none
Transmembrane domains: none
PFAM domains: predicted Ets-domain 294-373; SAM_PNT: 122-206
Summary: ERG2 is a sequence-specific DNA-binding protein.

```
MIQTVPDPAA HIKEALSVVS EDQSLFECAY GTPHLAKTEM TASSSSDYGQ TSKMSPRVPQ     60
QDWLSQPPAR VTIKMECNPS QVNGSRNSPD ECSVAKGGKM VGSPDTVGMN YGSYMEEKHM    120
PPPNMTTNER RVIVPADPTL WSTDHVRQWL EWAVKEYGLP DVNILLFQNI DGKELCKMTK    180
DDFQRLTPSY NADILLSHLH YLRETPLPHL TSDDVDKALQ NSPRLMHARN TDLPYEPPRR    240
SAWTGHGHPT PQSKAAQPSP STVPKTEDQR PQLDPYQILG PTSSRLANPG SGQIQLWQFL    300
LELLSDSSNS SCITWEGTNG EFKMTDPDEV ARRWGERKSK PNMNYDKLSR ALRYYYDKNI    360
MTKVHGKRYA YKFDFHGIAQ ALQPHPPESS LYKYPSDLPY MGSYHAHPQK MNFVAPHPPA    420
LPVTSSSFFA APNPYWNSPT GGIYPNTRLP TSHMPSHLGT YY                       462
```

AAD5 Protein sequence
Gene name: activin A receptor type II-like 1 (ALK-1)
Unigene number: Hs.172670
Probeset Accession #: T57112
Protein Accession #: NP_000011
Signal sequence: predicted 1-21
Transmembrane domain: predicted 119-135
PFAM domains: predicted pkinase 204-489
Summary: Type IA membrane protein; receptor tyrosine kinase

```
MTLGSPRKGL LMLLMALVTQ GDPVKPSRGP LVTCTCESPH CKGPTCRGAW CTVVLVREEG     60
RHPQEHRGCG NLHRELCRGR PTEFVNHYCC DSHLCNHNVS LVLEATQPPS EQPGTDGQLA    120
LILGPVLALL ALVALGVLGL WHVRRRQEKQ RGLHSELGES SLILKASEQG DTMLGDLLDS    180
DCTTGSGSGL PFLVQRTVAR QVALVECVGK GRYGEVWRGL WHGESVAVKI FSSRDEQSWF    240
RETEIYNTVL LRHDNILGFI ASDMTSRNSS TQLWLITHYH EHGSLYDFLQ RQTLEPHLAL    300
RLAVSAACGL AHLHVEIFGT QGKPAIAHRD FKSRNVLVKS NLQCCIADLG LAVMHSQGSD    360
YLDIGNNPRV GTKRYMAPEV LDEQIRTDCF ESYKWTDIWA FGLVLWEIAR RTIVNGIVED    420
YRPPFYDVVP NDPSFEDMKK VVCVDQQTPT IPNRLAADPV LSGLAQMMRE CWYPNPSARL    480
TALRIKKTLQ KISNSPEKPK VIQ
```

AAD8 Protein sequence
Gene name: ESTs
Unigene number: Hs.144953
Probeset Accession #: AA404418

Protein Accession #: n/a
Signal sequence: n/a
Transmembrane domains: n/a
PFAM domains: n/a
Summary: no ORF identified; possible frameshifts. Nearby to PCTAIRE protein kinase 2 (PCTK2) on the genome (within 100 kb).

ACA2 Protein sequence
Gene name: EST
Unigene number: Hs.16450
Probeset Accession #: AA478778
Protein Accession #: n/a
Signal sequence: n/a
Transmembrane domains: n/a
PFAM domains: n/a
Summary: no ORF identified, possible frameshifts; although a match was found to the HTGS genomic sequence, the sequence does not extend far enough upstream to predict coding exons.

ACA4 Protein sequence
Gene name: alpha satellite junction DNA sequence
Unigene number: Hs.247946
Probeset Accession #: M21305
Protein Accession #: AAA88020
Signal sequence: none
Transmembrane domains: none
PFAM domains: none

MEWNGMAWNR IKWNGINSSG MEWNGMEWNA VQCNRMEWNE LELTGMEWNG MHLN

ACG6 Protein sequence
Gene name: intercellular adhesion molecule 2 (ICAM2)
Unigene number: Hs.83738
Probeset Accession #: M32334
Protein Accession #: NP_000864
Signal sequence: predicted 1-21
Transmembrane domain: predicted 224-248
PFAM domains: predicted 41-98, 127-197; immunoglobulin-like C2-type domains
Summary: a predicted Type Ia membrane protein; it plays a role in cell adhesion and is the ligand for the LFA-1 protein. ICAM2 is also called CD102.

MSSFGYRTLT VALFTLICCP GSDEKVFEVH VRPKKLAVEP KGSLEVNCST TCNQPEVGGL 60
ETSLNKILLD EQAQWKHYLV SNISHDTVLQ CHFTCSGKQE SMNSNVSVYQ PPRQVILTLQ 120
PTLVAVGKSF TIECRVPTVE PLDSLTLFLF RGNETLHYET FGKAAPAPQE ATATFNSTAD 180
REDGHRNFSC LAVLDLMSRG GNIFHKHSAP KMLEIYEPVS DSQMVIIVTV VSVLLSLFVT 240
SVLLCFIFGQ HLRQQRMGTY GVRAAWRRLP QAFRP

ACG7 Protein sequence
Gene name: Cadherin 5, VE-cadherin (CDH5)
Unigene number: Hs.76206
Probeset Accession #: X79981
Protein Accession #: NP_001786
Signal sequence: predicted 1-27
Transmembrane domain: predicted 604-620
PFAM domains: Cadherin domains predicted 53-141, 156-249, 263-364, 377-470, and 487-576
Summary: Likely a Type I membrane protein. Cadherins are calcium-dependent adhesive proteins that mediate cell-to-cell interaction. VE-cadherin is associated with intercellular junctions.

MQRLMMLLAT SGACLGLLAV AAVAAAGANP AQRDTHSLLP THRRQKRDWI WNQMHIDEEK 60
NTSLPHHVGK IKSSVSRKNA KYLLKGEYVG KVFRVDAETG DVFAIERLDR ENISEYHLTA 120
VIVDKDTGEN LETPSSFTIK VHDVNDNWPV FTHRLFNASV PESSAVGTSV ISVTAVDADD 180
PTVGDHASVM YQILKGKEYF AIDNSGRIIT ITKSLDREKQ ARYEIVVEAR DAQGLRGDSG 240
TATVLVTLQD INDNFPFFTQ TKYTFVVPED TRVGTSVGSL FVEDPDEPQN RMTKYSILRG 300

DYQDAFTIET NPAHNEGIIK PMKPLDYEYI QQYSFIVEAT DPTIDLRYMS PPAGNRAQVI 360
INITDVDEPP IFQQPFYHFQ LKENQKKPLI GTVLAMDPDA ARHSIGYSIR RTSDKGQFFR 420
VTKKGDIYNE KELDREVYPW YNLTVEAKEL DSTGTPTGKE SIVQVHIEVL DENDNAPEFA 480
KPYQPKVCEN AVHGQLVLQI SAIDKDITPR NVKFKFTLNT ENNFTLTDNH DNTANITVKY 540
GQFDREHTKV HFLPVVISDN GMPSRTGTST LTVAVCKCNE QGEFTFCEDM AAQVGVSIQA 600
VVAILLCILT ITVITLLIFL RRRLRKQARA HGKSVPEIHE QLVTYDEEGG GEMDTTSYDV 660
SVLNSVRRGG AKPPRPALDA RPSLYAQVQK PPRHAPGAHG GPGEMAAMIE VKKDEADHDG 720
DGPPYDTLHI YGYEGSESIA ESLSSLGTDS SDSDVDYDFL NDWGPRFKML AELYGSDPRE 780
ELLY

ACG9 Protein sequence
Gene name: lysyl oxidase-like 2 (LOXL2)
Unigene number: Hs.83354
Probeset Accession #: U89942
Protein Accession #: NP_002309
Signal sequence: predicted 1-25
Transmembrane domains: none predicted
PFAM domains: scavenger receptor cysteine-rich domains predicted 68-159, 203-238, 336-425, 439-528; lysyl oxidase predicted 548-749.
Summary: Likely a secreted protein. Lysyl oxidase is a copper-dependent amine oxidase that belongs to a heterogeneous family of enzymes that oxidize primary amine substrates to reactive aldehydes, acting on the extracellular matrix substrates, e.g., collagen and elastin.

MERPLCSHLC SCLAMLALLS PLSLAQYDSW PHYPEYFQQP APEYHQPQAP ANVAKIQLRL 60
AGQKRKHSEG RVEVYYDGQW GTVCDDDFSI HAAHVVCREL GYVEAKSWTA SSSYGKGEGP 120
IWLDNLHCTG NEATLAACTS NGWGVTDCKH TEDVGVVCSD KRIPGFKFDN SLINQIENLN 180
IQVEDIRIRA ILSTYRKRTP VMEGYVEVKE GKTWKQICDK HWTAKNSRVV CGMFGFPGER 240
TYNTKVYKMF ASRRKQRYWP FSMDCTGTEA HISSCKLGPQ VSLDPMKNVT CENGLPAVVS 300
CVPGQVFSPD GPSRFRKAYK PEQPLVRLRG GAYIGEGRVE VLKNGEWGTV CDDKWDLVSA 360
SVVCRELGFG SAKEAVTGSR LGQGIGPIHL NEIQCTGNEK SIIDCKFNAE SQGCNHEEDA 420
GVRCNTPAMG LQKKLRLNGG RNPYEGRVEV LVERNGSLVW GMVCGQNWGI VEAMVVCRQL 480
GLGFASNAFQ ETWYWHGDVN SNKVVMSGVK CSGTELSLAH CRHDGEDVAC PQGGVQYGAG 540
VACSETAPDL VLNAEMVQQT TYLEDRPMFM LQCAMEENCL SASAAQTDPT TGYRRLLRFS 600
SQIHNNGQSD FRPKNGRHAW IWHDCHRHYH SMEVFTHYDL LNLNGTKVAE GHKASFCLED 660
TECEGDIQKN YECANFGDQG ITMGCWDMYR HDIDCQWVDI TDVPPGDYLF QVVINPNFEV 720
AESDYSNNIM KCRSRYDGHR IWMYNCHIGG SFSEETEKKF EHFSGLLNNQ LSPQ

ACH2 Protein sequence
Gene name: TIE tyrosine-protein kinase
Unigene number: Hs.78824
Probeset Accession #: M60957
Protein Accession #: NP_005415
Signal sequence: predicted 1-21
Transmembrane domain: predicted 770-786
PFAM domains: laminin-EGF predicted 234-267; FN3 predicted 460-520, 548-632, and 644-729; tyrosine_kinase predicted 839-1107
Summary: Likely a Type Ia membrane protein; TIE is a tyrosine-kinase receptor with an unknown ligand; its expression is likely necessary for normal blood vessel development.

MVWRVPPFLL PILFLASHVG AAVDLTLLAN LRLTDPQRFF LTCVSGEAGA GRGSDAWGPP 60
LLLEKDDRIV RTPPGPPLRL ARNGSHQVTL RGFSKPSDLV GVFSCVGGAG ARRTRVIYVH 120
NSPGAHLLPD KVTHTVNKGD TAVLSARVHK EKQTDVIWKS NGSYFYTLDW HEAQDGRFLL 180
QLPNVQPPSS GIYSATYLEA SPLGSAFFRL IVRGCGAGRW GPGCTKECPG CLHGGVCHDH 240
DGECVCPPGF TGTRCEQACR EGRFGQSCQE QCPGISGCRG LTFCLPDPYG CSCGSGWRGS 300
QCQFTCAPGH FGADCRLQCQ CQNGGTCDRF SGCVCPSGWH GVHCEKSDRI PQILNMASEL 360
EFNLTMPRI NCAAAGNPFP VRGSIELRKP DGTVLLSTKA IVEPEKTTAE FEVPRLVLAD 420
SGFWECRVST SGGQDSRRFK VNVKVPPVPL AAPRLLTKQS RQLVVSPLVS FSGDGPISTV 480
RLHYRPQDST MDWSTIVVDP SENVTLMNLR PKTGYSVRVQ LSRPGEGGEG AWGPPTLMTT 540
DCPEPLLQPW LEGWHVEGTD RLRVSWSLPL VPGPLVGDGF LLRLWDGTRG QERRENVSSP 600
QARTALLTGL TPGTHYQLDV QLYHCTLLGP ASPPAHVLLP PSGPPAPRHL HAQALSDSEI 660
QLTWKHPEAL PGPISKYVVE VQVAGGAGDP LWIDVDRPEE TSTIIRGLNA STRYLFRMRA 720
SIQGLGDWSN TVEESTLGNG LQAEGPVQES RAAEEGLDQQ LILAVVGSVS ATCLTILAAL 780
LTLVCIRRSC LHRRRTFTYQ SGSGEETILQ FSSGTLTLTR RPKLQPEPLS YPVLEWEDIT 840
FEDLIGEGNF GQVIRAMIKK DGLKMNAAIK MLKEYASEND HRDFAGELEV LCKLGHHPNI 900

INLLGACKNR GYLYIAIEYA PYGNLLDFLR KSRVLETDPA FAREHGTAST LSSRQLLRFA 960
SDAANGMQYL SEKQFIHRDL AARNVLVGEN LASKIADFGL SRGEEVYVKK TMGRLPVRWM 1020
AIESLNYSVY TTKSDVWSFG VLLWEIVSLG GTPYCGMTCA ELYEKLPQGY RMEQPRNCDD 1080
EVYELMRQCW RDRPYERPPF AQIALQLGRM LEARKAYVNM SLFENFTYAG IDATAEEA

ACH3 Protein sequence
Gene name: placental growth factor (PGF; PlGF1; VEGF-related protein)
Unigene number: Hs.2894
Probeset Accession #: X54936
Protein Accession #: NP_002623
Signal sequence: predicted 1-21
Transmembrane domain: none predicted
PFAM domains: PDGF predicted 52-130
Summary: Likely a secreted protein; likely regulates angiogenesis by interacting with FLT1 and FLK1.

MPVMRLFPCF LQLLAGLALP AVPPQQWALS AGNGSSEVEV VPFQEVWGRS YCRALERLVD 60
VVSEYPSEVE HMFSPSCVSL LRCTGCCGDE NLHCVPVETA NVTMQLLKIR SGDRPSYVEL 120
TFSQHVRCEC RPLREKMKPE RCGDAVPRR

ACH4 Protein sequence
Gene name: nidogen 2 (NID2)
Unigene number: Hs.82733
Probeset Accession #: D86425
Protein Accession #: NP_031387
Signal sequence: predicted 1-30
Transmembrane domain: none predicted
PFAM domains: EGF-like_domains predicted 489-524, 764-800, 806-843, 853-891, and 897-930; thyroglobulin_repeats predicted 941-1006, and 1020-1085; LDL_receptor_repeats predicted 1155-1197, 1199-1240, and 1242-1285.
Summary: A secreted protein; NID2 likely interacts with collagens I and IV and laminin-1 to promote cell adhesion to the basement membrane.

MEGDRVAGRP VLSSLPVLLL LQLLMLRAAA LHPDELFPHG ESWWDQLLQE GDDVKLSRGE 60
AGESPALLTK PDSATSTWAP TASSPLRTSP GKRSMWTMIS PPTSRPSPLF WRTSTRATAE 120
AESCTERTPP PQCWAWPPAM CALASRALRA FYPHPRLPGH LGAGRRLRGG QTRALPSGEL 180
NTFQAVLASD GSDSYALFLY PANGLQFLGT RPKESYNVQL QLPARVGFCR GEADDLKSEG 240
PYFSLTSTEQ SVKNLYQLSN LGIPGVWAFH IGSTSPLDNV RPAAVGDLSA AHSSVPLGRS 300
FSHATALESD YNEDNLDYYD VNEEEAEYLP GEPEEALNGH SSIDVSFQSK VDTKPLEESS 360
TLDPHTKEGT SLGEVGGPDL KGQVEPWDER ETRSPAPPEV DRDSLAPSWE TPPPYPENGS 420
IQPYPDGGPV PSEMDVPPAH PEEEIVLRSY PASGHTTPLS RGTYEVGLED NIGSNTEVFT 480
YNAANKETCE HNHRQCSRHA FCTDYATGFC CHCQSKFYGN GKHCLPEGAP HRVNGKVSGH 540
LHVGHTPVHF TDVDLHAYIV GNDGRAYTAI SHIPQPAAQA LLPLTPIGGL FGWLFALEKP 600
GSENGFSLAG AAFTHDMEVT FYPGEETVRI TQTAEGLDPE NYLSIKTNIQ GQVPYVPANF 660
TAHISPYKEL YHYSDSTVTS TSSRDYSLTF GAINQTWSYR IHQNITYQVC RHAPRHPSFP 720
TTQQLNVDRV FALYNDEERV LRFAVTNQIG PVKEDSDPTP VNPCYDGSHM CDTTARCHPG 780
TGVDYTCECA SGYQGDGRNC VDENECATGF HRCGPNSVCI NLPGSYRCEC RSGYEFADDR 840
HTCILITPPA NPCEDGSHTC APAGQARCVH HGGSTFSCAC LPGYAGDGHQ CTDVDECSEN 900
RCHPAATCYN TPGSFSCRCQ PGYYGDGFQC IPDSTSSLTP CEQQQRHAQA QYAYPGARFH 960
IPQCDEQGNF LPLQCHGSTG FCWCVDPDGH EVPGTQTPPG STPPHCGPSP EPTQRPPTIC 1020
ERWRENLLEH YGGTPRDDQY VPQCDDLGHF IPLQCHGKSD FCWCVDKDGR EVQGTRSQPG 1080
TTPACIPTVA PPMVRPTPRP DVTPPSVGTF LLYTQGQQIG YLPLNGTRLQ KDAAKTLLSL 1140
HGSIIVGIDY DCRERMVYWT DVAGRTISRA GLELGAEPET IVNSGLISPE GLAIDHIRRT 1200
MYWTDSVLDK IESALLDGSE RKVLFYTDLV NPRAIAVDPI RGNLYWTDWN REAPKIETSS 1260
LDGENRRILI NTDIGLPNGL TFDPFSKLLC WADAGTKKLE CTLPDGTGRR VIQNNLKYPF 1320
SIVSYADHFY HTDWRRDGVV SVNKHSGQFT DEYLPEQRSH LYGITAVYPY CPTGRK

ACH5 Protein sequence
Gene name: SNL (singed-like; sea urchin fascin homolog-like)
Unigene number: Hs.118400
Probeset Accession #: U03057
Protein Accession #: NP_003079
Signal sequence: none identified
Transmembrane domain: none identified
PFAM domains: none identified

Summary: a cytoplasmic, actin-bundling protein that is likely to be involved in the assembly of actin filament bundles present in microspikes, membrane ruffles, and stress fibers

```
MTANGTAEAV QIQFGLINCG NKYLTAEAFG FKVNASASSL KKKQIWTLEQ PPDEAGSAAV    60
CLRSHLGRYL AADKDGNVTC EREVPGPDCR FLIVAHDDGR WSLQSEAHRR YFGGTEDRLS   120
CFAQTVSPAE KWSVHIAMHP QVNIYSVTRK RYAHLSARPA DEIAVDRDVP WGVDSLITLA   180
FQDQRYSVQT ADHRFLRHDG RLVARPEPAT GYTLEFRSGK VAFRDCEGRY LAPSGPSGTL   240
KAGKATKVGK DELFALEQSC AQVVLQAANE RNVSTRQGMD LSANQDEETD QETFQLEIDR   300
DTKKCAFRTH TGKYWTLTAT GGVQSTASSK NASCYFDIEW RDRRITLRAS NGKFVTSKKN   360
GQLAASVETA GDSELFLMKL INRPIIVFRG EHGFIGCRKV TGTLDANRSS YDVFQLEFND   420
GAYNIKDSTG KYWTVGSDSA VTSSGDTPVD FFFEFCDYNK VAIKVGGRYL KGDHAGVLKA   480
SAETVDPASL WEY
```

ACH6 Protein sequence
Gene name: endothelial protein C receptor (EPCR; PROCR)
Unigene number: Hs.82393
Probeset Accession #: L35545
Protein Accession #: NP_006395
Signal sequence: predicted 1-17
Transmembrane domain: predicted 211-227
PFAM domains: none identified
Summary: a Type Ia membrane protein, EPCR likely binds to [thrombin]-activated Protein C, a vitamin K-dependent serine protease zymogen necessary for blood coagulation.

```
MLTTLLPILL LSGWAFCSQD ASDGLQRLHM LQISYFRDPY HVWYQGNASL GGHLTHVLEG    60
PDTNTTIIQL QPLQEPESWA RTQSGLQSYL LQFHGLVRLV HQERTLAFPL TIRCFLGCEL   120
PPEGSRAHVF FEVAVNGSSF VSFRPERALW QADTQVTSGV VTFTLQQLNA YNRTRYELRE   180
FLEDTCVQYV QKHISAENTK GSQTSRSYTS LVLGVLVGGF IIAGVAVGIF LCTGGRRC
```

ACH8 Protein sequence
Gene name: melanoma adhesion molecule (MCAM; MUC18)
Unigene number: Hs.211579
Probeset Accession #: D51069
Protein Accession #: NP_006491
Signal sequence: predicted 1-17
Transmembrane domain: predicted 559-575
PFAM domains: immunoglobulin domains predicted 264-324, and 356-410.
Summary: a Type Ia membrane protein, associated with tumor progression and the development of metastasis in human malignant melanoma, and may play a role in neural crest cells during embryonic development.

```
MGLPRLVCAF LLAACCCCPR VAGVPGEAEQ PAPELVEVEV GSTALLKCGL SQSQGNLSHV    60
DWFSVHKEKR TLIFRVRQGQ GQSEPGEYEQ RLSLQDRGAT LALTQVTPQD ERIFLCQGKR   120
PRSQEYRIQL RVYKAPEEPN IQVNPLGIPV NSKEPEEVAT CVGRNGYPIP QVIWYKNGRP   180
LKEEKNRVHI QSSQTVESSG LYTLQSILKA QLVKEDKDAQ FYCELNYRLP SGNHMKESRE   240
VTVPVFYPTE KVWLEVEPVG MLKEGDRVEI RCLADGNPPP HFSISKQNPS TREAEEETTN   300
DNGVLVLEPA RKEHSGRYEC QAWNLDTMIS LLSEPQELLV NYVSDVRVSP AAPERQEGSS   360
LTLTCEAESS QDLEFQWLRE ETDQVLERGP VLQLHDLKRE AGGGYRCVAS VPSIPGLNRT   420
QLVKLAIFGP PWMAFKERKV WVKENMVLNL SCEASGHPRP TISWNVNGTA SEQDQDPQRV   480
LSTLNVLVTP ELLETGVECT ASNDLGKNTS ILFLELVNLT TLTPDSNTTT GLSTSTASPH   540
TRANSTSTER KLPEPESRGV VIVAVIVCIL VLAVLGAVLY FLYKKGKLPC RRSGKQEITL   600
PPSRKTELVV EVKSDKLPEE MGLLQGSSGD KRAPGDQGEK YIDLRH
```

ACH9 Protein sequence
Gene name: endothelin-1 (EDN1)
Unigene number: Hs.2271
Probeset Accession #: J05008
Protein Accession #: NP_001946
Signal sequence: predicted 1-17
Transmembrane domain: none predicted
PFAM domains: Endothelin domains predicted 59-73, and 108-129.

Summary: a secreted zymogen; the active protein is likely a 26-amino acid peptide with potent mammalian vasoconstrictor activity; it is necessary for normal vessel development.

```
MDYLLMIFSL LFVACQGAPE TAVLGAELSA VGENGGEKPT PSPPWRLRRS KRCSCSSLMD    60
KECVYFCHLD IIWVNTPEHV VPYGLGSPRS KRALENLLPT KATDRENRCQ CASQKDKKCW   120
NFCQAGKELR AEDIMEKDWN NHKKGKDCSK LGKKCIYQQL VRGRKIRRSS EEHLRQTRSE   180
TMRNSVKSSF HDPKLKGKPS RERYVTHNRA HW
```

ACJ1 Protein sequence
Gene name: BMX non-receptor tyrosine kinase
Unigene number: Hs.27372
Probeset Accession #: X83107
Protein Accession #: NP_001712
Signal sequence: none identified
Transmembrane domain: none identified
PFAM domains: plektrin_homology_domain predicted 6-111; SH2_domain predicted 294-383; protein_kinase_domain predicted 417-663
Summary: a cytoplasmic protein, it likely plays a role in the growth and differentiation of hematopoietic cells; it is known to also be expressed in endothelial cells.

```
MDTKSILEEL LLKRSQQKKK MSPNNYKERL FVLTKTNLSY YEYDKMKRGS RKGSIEIKKI    60
RCVEKVNLEE QTPVERQYPF QIVYKDGLLY VYASNEESRS QWLKALQKEI RGNPHLLVKY   120
HSGFFVDGKF LCCQQSCKAA PGCTLWEAYA NLHTAVNEEK HRVPTFPDRV LKIPRAVPVL   180
KMDAPSSSTT LAQYDNESKK NYGSQPPSSS TSLAQYDSNS KKIYGSQPNF NMQYIPREDF   240
PDWWQVRKLK SSSSSEDVAS SNQKERNVNH TTSKISWEFP ESSSSEEEEN LDDYDWFAGN   300
ISRSQSEQLL RQKGKEGAFM VRNSSQVGMY TVSLFSKAVN DKKGTVKHYH VHTNAENKLY   360
LAENYCFDSI PKLIHYHQHN SAGMITRLRH PVSTKANKVP DSVSLGNGIW ELKREEITLL   420
KELGSGQFGV VQLGKWKGQY DVAVKMIKEG SMSEDEFFQE AQTMMKLSHP KLVKFYGVCS   480
KEYPIYIVTE YISNGCLLNY LRSHGKGLEP SQLLEMCYDV CEGMAFLESH QFIHRDLAAR   540
NCLVDRDLCV KVSDFGMTRY VLDDQYVSSV GTKFPVKWSA PEVFHYFKYS SKSDVWAFGI   600
LMWEVFSLGK QPYDLYDNSQ VVLKVSQGHR LYRPHLASDT IYQIMYSCWH ELPEKRPTFQ   660
QLLSSIEPLR EKDKH
```

ACJ4 Protein sequence
Gene name: prostaglandin G/H synthase 2 (COX-2; PGHS-2)
Unigene number: Hs.196384
Probeset Accession #: D28235
Protein Accession #: NP_000954
Signal sequence: predicted 1-17
Transmembrane domain: none identified
PFAM domains: EGF-like_domain predicted 18-55.
Summary: a microsomal enzyme; COX-2 is the therapeutic target of the nonsteroidal anti-inflammatory drugs (NSAIDs), such as aspirin.

```
MLARALLLCA VLALSHTANP CCSHPCQNRG VCMSVGFDQY KCDCTRTGFY GENCSTPEFL    60
TRIKLFLKPT PNTVHYILTH FKGFWNVVNN IPFLRNAIMS YVLTSRSHLI DSPPTYNADY   120
GYKSWEAFSN LSYYTRALPP VPDDCPTPLG VKGKKQLPDS NEIVEKLLLR RKFIPDPQGS   180
NMMFAFFAQH FTHQFFKTDH KRGPAFTNGL GHGVDLNHIY GETLARQRKL RLFKDGKMKY   240
QIIDGEMYPP TVKDTQAEMI YPPQVPEHLR FAVGQEVFGL VPGLMMYATI WLREHNRVCD   300
VLKQEHPEWG DEQLFQTSRL ILIGETIKIV IEDYVQHLSG YHFKLKFDPE LLFNKQFQYQ   360
NRIAAEFNTL YHWHPLLPDT FQIHDQKYNY QQFIYNNSIL LEHGITQFVE SFTRQIAGRV   420
AGGRNVPPAV QKVSQASIDQ SRQMKYQSFN EYRKRFMLKP YESFEELTGE KEMSAELEAL   480
YGDIDAVELY PALLVEKPRP DAIFGETMVE VGAPFSLKGL MGNVICSPAY WKPSTFGGEV   540
GFQIINTASI QSLICNNVKG CPFTSFSVPD PELIKTVTIN ASSSRSGLDD INPTVLLKER   600
STEL
```

ACJ6 Protein sequence
Gene name: SEC14-like 1
Unigene number: Hs.75232
Probeset Accession #: D67029
Protein Accession #: NP_002994
Signal sequence: none identified
Transmembrane domain: none identified

PFAM domains: none identified
Summary: a cytoplasmic protein

```
MVQKYQSPVR VYKYPFELIM AAYERRFPTC PLIPMFVGSD TVSEFKSEDG AIHVIERRCK    60
LDVDAPRLLK KIAGVDYVYF VQKNSLNSRE RTLHIEAYNE TFSNRVIINE HCCYTVHPEN   120
EDWTCFEQSA SLDIKSFFGF ESTVEKIAMK QYTSNIKKGK EIIEYYLRQL EEEGITFVPR   180
WSPPSITPSS ETSSSSSKKQ AASMAVVIPE AALKEGLSGD ALSSPSAPEP VVGTPDDKLD   240
ADHIKRYLGD LTPLQESCLI RLRQWLQETH KGKIPKDEHI LRFLRARDFN IDKAREIMCQ   300
SLTWRKQHQV DYILETWTPP QVLQDYYAGG WHHHDKDGRP LYVLRLGQMD TKGLVRALGE   360
EALLRYVLSV NEERLRRCEE NTKVFGRPIS SWTCLVDLEG LNMRHLWRPG VKALLRIIEV   420
VEANYPETLG RLLILRAPRV FPVLWTLVSP FIDDNTRRKF LIYAGNDYQG PGGLLDYIDK   480
EIIPDFLSGE CMCEVPEGGL VPKSLYRTAE ELENEDLKLW TETIYQSASV FKGAPHEILI   540
QIVDASSVIT WDFDVCKGDI VFNIYHSKRS PQPPKKDSLG AHSITSPGGN NVQLIDKVWQ   600
LGRDYSMVES PLICKEGESV QGSHVTRWPG FYILQWKFHS MPACAASSLP RVDDVLASLQ   660
VSSHKCKVMY YTEVIGSEDF RGSMTSLESS HSGFSQLSAA TTSSSQSHSS SMISR
```

ACJ8 Protein sequence
Gene name: intercellular adhesion molecule 1 (ICAM1; CD54)
Unigene number: Hs.168383
Probeset Accession #: M24283
Protein Accession #: NP_000192
Signal sequence: predicted 1-27
Transmembrane domain: predicted 481-497
PFAM domains: Immunoglobulin_domains predicted 128-188, and 325-373.
Summary: a Type 1a membrane protein; ICAM1 is typically expressed on endothelial cells and cells of the immune system; ICAM1 binds to integrins of type CD11a/CD18, or CD11b/CD18; ICAM1 is also exploited by Rhinovirus as a receptor.

```
MAPSSPRPAL PALLVLLGAL FPGPGNAQTS VSPSKVILPR GGSVLVTCST SCDQPKLLGI    60
ETPLPKKELL LPGNNRKVYE LSNVQEDSQP MCYSNCPDGQ STAKTFLTVY WTPERVELAP   120
LPSWQPVGKN LTLRCQVEGG APRANLTVVL LRGEKELKRE PAVGEPAEVT TTVLVRRDHH   180
GANFSCRTEL DLRPQGLELF ENTSAPYQLQ TFVLPATPPQ LVSPRVLEVD TQGTVVCSLD   240
GLFPVSEAQV HLALGDQRLN PTVTYGNDSF SAKASVSVTA EDEGTQRLTC AVILGNQSQE   300
TLQTVTIYSF PAPNVILTKP EVSEGTEVTV KCEAHPRAKV TLNGVPAQPL GPRAQLLLKA   360
TPEDNGRSFS CSATLEVAGQ LIHKNQTREL RVLYGPRLDE RDCPGNWTWP ENSQQTPMCQ   420
AWGNPLPELK CLKDGTFPLP IGESVTVTRD LEGTYLCRAR STQGEVTREV TVNVLSPRYE   480
IVIITVVAAA VIMGTAGLST YLYNRQRKIK KYRLQQAQKG TPMKPNTQAT PP
```

ACK3 Protein sequence
Gene name: angiopoietin 1 receptor (TIE-2; TEK)
Unigene number: Hs.89640
Probeset Accession #: L06139
Protein Accession #: NP_000450
Signal sequence: predicted 1-18
Transmembrane domain: predicted 746-770
PFAM domains: immunoglobulin_domains predicted 44-102, 370-424; EGF_like_domains predicted 210-252, 254-299, and 301-341; FN3_domains predicted 444-536, 541-634, and 638-732; protein_kinase_domain predicted 824-1096.
Summary: a Type 1a membrane protein; it is expressed almost exclusively in endothelial cells in mice, rats, and humans; the ligand for this receptor is angiopoietin-1; defects in TEK are associated with inherited venous malformations; the TEK signaling pathway appears to be critical for endothelial cell-smooth muscle cell communication in venous morphogenesis.

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MDSLASLVLC GVSLLLSGTV EGAMDLILIN SLPLVSDAET SLTCIASGWR PHEPITIGRD    60
FEALMNQHQD PLEVTQDVTR EWAKKVVWKR EKASKINGAY FCEGRVRGEA IRIRTMKMRQ   120
QASFLPATLT MTVDKGDNVN ISFKKVLIKE EDAVIYKNGS FIHSVPRHEV PDILEVHLPH   180
AQPQDAGVYS ARYIGGNLFT SAFTRLIVRR CEAQKWGPEC NHLCTACMNN GVCHEDTGEC   240
ICPPGFMGRT CEKACELHTF GRTCKERCSG QEGCKSYVFC LPDPYGCSCA TGWKGLQCNE   300
ACHPGFYGPD CKLRCSCNNG EMCDRFQGCL CSPGWQGLQC EREGIPRMTP KIVDLPDHIE   360
VNSGKFNPIC KASGWPLPTN EEMTLVKPDG TVLHPKDFNH TDHFSVAIFT IHRILPPDSG   420
VWVCSVNTVA GMVEKPFNIS VKVLPKPLNA PNVIDTGHNF AVINISSEPY FGDGPIKSKK   480
LLYKPVNHYE AWQHIQVTNE IVTLNYLEPR TEYELCVQLV RRGEGGEGHP GPVRRFTTAS   540
IGLPPPRGLN LLPKSQTTLN LTWQPIFPSS EDDFYVEVER RSVQKSDQQN IKVPGNLTSV   600
LLNNLHPREQ YVVRARVNTK AQGEWSEDLT AWTLSDILPP QPENIKISNI THSSAVISWT   660
ILDGYSISSI TIRYKVQGKN EDQHVDVKIK NATIIQYQLK GLEPETAYQV DIFAENNIGS   720
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SNPAFSHELV TLPESQAPAD LGGGKMLLIA ILGSAGMTCL TVLLAFLIIL QLKRANVQRR 780
MAQAFQNVRE EPAVQFNSGT LALNRKVKNN PDPTIYPVLD WNDIKFQDVI GEGNFGQVLK 840
ARIKKDGLRM DAAIKRMKEY ASKDDHRDFA GELEVLCKLG HHPNIINLLG ACEHRGYLYL 900
AIEYAPHGNL LDFLRKSRVL ETDPAFAIAN STASTLSSQQ LLHFAADVAR GMDYLSQKQF 960
IHRDLAARNI LVGENYVAKI ADFGLSRGQE VYVKKTMGRL PVRWMAIESL NYSVYTTNSD 1020
VWSYGVLLWE IVSLGGTPYC GMTCAELYEK LPQGYRLEKP LNCDDEVYDL MRQCWREKPY 1080
ERPSFAQILV SLNRMLEERK TYVNTTLYEK FTYAGIDCSA EEAA

PZA6 Protein sequence
Gene name: prostate differentiation factor (PLAB; MIC-1)
Unigene number: Hs.116577
Probeset Accession #: AB000584
Protein Accession #: NP_004855
Signal sequence: predicted 1-29
Transmembrane domain: none identified
PFAM domains: TGF_beta _domain predicted 211-308.
Summary: a secreted protein; its exact function is unclear; it inhibits proliferation of primitive hematopoietic progenitors; it inhibits activation of macrophages; it is highly expressed in placenta and in serum of pregnant women; it may promote fetal survival by suppressing the production of maternally-derived proinflammatory cytokines within the uterus.

MPGQELRTVN GSQMLLVLLV LSWLPHGGAL SLAEASRASF PGPSELHSED SRFRELRKRY 60
EDLLTRLRAN QSWEDSNTDL VPAPAVRILT PEVRLGSGGH LHLRISRAAL PEGLPEASRL 120
HRALFRLSPT ASRSWDVTRP LRRQLSLARP QAPALHLRLS PPPSQSDQLL AESSSARPQL 180
ELHLRPQAAR GRRRARARNG DDCPLGPGRC CRLHTVRASL EDLGWADWVL SPREVQVTMC 240
IGACPSQFRA ANMHAQIKTS LHRLKPDTEP APCCVPASYN PMVLIQKTDT GVSLQTYDDL 300
LAKDCHCI

AAD2 Protein sequence:
Gene name: Thrombospondin-1
Unigene number: Hs.87409
Probeset Accession #: AA232645
Protein Accession #: NP_003237.1
Signal sequence: predicted 1-18 (first underlined sequence)
Transmembrane Domain: none identified
Summary: Thrombospondin is a large modular glycoprotein component of the extracellular matrix and contains a variety of distinct domains, including three repeating subunits (types I, II, and III) that share homology to an assortment of other proteins.

MGLAWGLGVL FLMHVCGTNR IPESGGDNSV FDIFELTGAA RKGSGRRLVK GPDPSSPAFR 60
IEDANLIPPV PDDKFQDLVD AVRAEKGFLL LASLRQMKKT RGTLLALERK DHSGQVFSVV 120
SNGKAGTLDL SLTVQGKQHV VSVEEALLAT GQWKSITLFV QEDRAQLYID CEKMENAELD 180
VPIQSVFTRD LASIARLRIA KGGVNDNFQG VLQNVRFVFG TTPEDILRNK GCSSSTSVLL 240
TLDNNVVNGS SPAIRTNYIG HKTKDLQAIC GISCDELSSM VLELRGLRTI VTTLQDSIRK 300
VTEENKELAN ELRRPPLCYH NGVQYRNNEE WTVDSCTECH CQNSVTICKK VSCPIMPCSN 360
ATVPDGECCP RCWPSDSADD GWSPWSEWTS CSTSCGNGIQ QRGRSCDSLN NRCEGSSVQT 420
RTCHIQECDK RFKQDGGWSH WSPWSSCSVT CGDGVITRIR LCNSPSPQMN GKPCEGEARE 480
TKACKKDACP INGGWGPWSP WDICSVTCGG GVQKRSRLCN NPAPQFGGKD CVGDVTENQI 540
CNKQDCPIDG CLSNPCFAGV KCTSYPDGSW KCGACPPGYS GNGIQCTDVD ECKEVPDACF 600
NHNGEHRCEN TDPGYNCLPC PPRFTGSQPF GQGVEHATAN KQVCKPRNPC TDGTHDCNKN 660
AKCNYLGHYS DPMYRCECKP GYAGNGIICG EDTDLDGWPN ENLVCVANAT YHCKKDNCPN 720
LPNSGQEDYD KDGIGDACDD DDDNDKIPDD RDNCPFHYNP AQYDYDRDDV GDRCDNCPYN 780
HNPDQADTDN NGEGDACAAD IDGDGILNER DNCQYVYNVD QRDTDMDGVG DQCDNCPLEH 840
NPDQLDSDSD RIGDTCDNNQ DIDEDGHQNN LDNCPYVPNA NQADHDKDGK GDACDHDDDN 900
DGIPDDKDNC RLVPNPDQKD SDGDGRGDAC KDDFDHDSVP DIDDICPENV DISETDFRRF 960
QMIPLDPKGT SQNDPNWVVR HQGKELVQTV NCDPGLAVGY DEFNAVDFSG TFFINTERDD 1020
DYAGFVFGYQ SSSRFYVVMW KQVTQSYWDT NPTRAQGYSG LSVKVVNSTT GPGEHLRNAL 1080
WHTGNTPGQV RTLWHDPRHI GWKDFTAYRW RLSHRPKTGF IRVVMYEGKK IMADSGPIYD 1140
KTYAGGRLGL FVFSQEMVFF SDLKYECRDP

AAD9 protein sequence
Gene name: LIM homeobox protein cofactor (CLIM-1)
Unigene number: Hs.4980

Probeset Accession #: F13782
Protein Accession #: AAC83552
Pfam: LIM bind
Transmembrane Domain: none identifed
Summary: The LIM homeodomain (LIM-HD) proteins, which contain two tandem LIM domains followed by a homeodomain, are critical transcriptional regulators of embryonic development. The LIM domain is a conserved cysteine-rich zinc-binding motif found in LIM-HD proteins, cytoskeletal components, LIM kinases, and other proteins. LIM domains are protein-protein interaction motifs, can inhibit binding of LIM-HD proteins to DNA, and can negatively regulate LIM-HD protein function.

MSSTPHDPFY SSPFGPFYRR HTPYMVQPEY RIYEMNKRLQ SRTEDSDNLW WDAFATEFFE 60
DDATLTLSFC LEDGPKRYTI GRTLIPRYFS TVFEGGVTDL YYILKHSKES YHNSSITVDC 120
DQCTMVTQHG KPMFTKVCTE GRLILEFTFD DLMRIKTWHF TIRQYRELVP RSILAMHAQD 180
PQVLDQLSKN ITRMGLTNFT LNYLRLCVIL EPMQELMSRH KTYNLSPRDC LKTCLFQKWQ 240
RMVAPPAEPT RQPTTKRRKR KNSTSSTSNS SAGNNANSTG SKKKTTAANL SLSSQVPDVM 300
VVGEPTLMGG EFGDEDERLI TRLENTQYDA ANGMDDEEDF NNSPALGNNS PWNSKPPATQ 360
ETKSENPPPQ ASQ

AAE1 protein sequence
Gene name: guanine nucleotide binding protein 11
Unigene number: Hs.83381
Probeset Accession #: U31384
Protein Accession #: NP_004117.1
Pfam: G-gamma; CAAX motif (farnesylation site) prediction underlined
Summary: The G gamma proteins are a component of the trimeric G-proteins that interact with cell surface receptors. The G protein beta and gamma subunits directly regulate the activities of various enzymes and ion channels after receptor ligation. Unlike most of the other known gamma subunits, gamma 11 is modified by a farnesyl group and is not capable of interacting with beta 2.

MPALHIEDLP EKEKLKMEVE QLRKEVKLQR QQVSKCSEEI KNYIEERSGE DPLVKGIPED 60
KNPFKEKGSC VIS

AAE2 protein sequence
Gene name: Transcription factor 4 (Immunoglobulin transcription factor 2)(ITF-2) (SL3-3 Enhancer factor 2) (SEF-2)
Unigene number: Hs.289068
Probeset Accession #: M74719
Protein Accession #: NP_003190.1
Pfam: HLH domain prediction underlined
Summary: Transcription factor 4 is a helix-loop-helix (HLH) protein which belongs to a family of nuclear proteins, designated SL3-3 enhancer factors 2 (SEF2), that interact with an Ephrussi box-like motif within the glucocorticoid response element in the enhancer of the murine leukemia virus SL3-3. Various cell types display differences both in the sets of SEF2-DNA complexes formed and in their amounts. Molecular analysis of cDNA clones show the existence of multiple related mRNA species containing alternative coding regions, which are most probably a result of differential splicing.

MHHQQRMAAL GTDKELSDLL DFSAMFSPPV SSGKNGPTSL ASGHFTGSNV EDRSSSGSWG 60
NGGHPSPSRN YGDGTPYDHM TSRDLGSHDN LSPPFVNSRI QSKTERGSYS SYGRESNLQG 120
CHQQSLLGGD MDMGNPGTLS PTKPGSQYYQ YSSNNPRRRP LHSSAMEVQT KKVRKVPPGL 180
PSSVYAPSAS TADYNRDSPG YPSSKPATST FPSSFFMQDG HHSSDPWSSS SGMNQPGYAG 240
MLGNSSHIPQ SSSYCSLHPH ERLSYPSHSS ADINSSLPPM STFHRSGTNH YSTSSCTPPA 300
NGTDSIMANR GSGAAGSSQT GDALGKALAS IYSPDHTNNS FSSNPSTPVG SPPSLSAGTA 360
VWSRNGGQAS SSPNYEGPLH SLQSRIEDRL ERLDDAIHVL RNHAVGPSTA MPAGHGDMHG 420
IIGPSHNGAM GGLGSGYGTG LLSANRHSLM VGTHREDGVA LRGSHSLLPN QVPVPQLPVQ 480
SATSPDLNPP QDPYRGMPPG LQGQSVSSGS SEIKSDDEGD ENLQDTKSSE DKKLDDDKKD 540
IKSITSNNDD EDLTPEQKAE REKERRMANN ARERLRVRDI NEAFKELGRM VQLHLKSDKP 600
QTKLLILHQA VAVILSLEQQ VRERNLNPKA ACLKRREEEK VSSEPPPLSL AGPHPGMGDA 660
SNHMGQM

AAE4 protein sequence

Gene name: phosphatidylcholine 2-acylhydrolase
Unigene number: Hs.211587
Probeset Accession #: M68874
Protein Accession #: AAA60105.1
Pfam: PLA2 B, C2 domain prediction underlined
Summary: Phospholipases A2 (PLA2s) play a key role in inflammatory processes through production of precursors of eicosanoids and platelet-activating factor. PLA2 is a 100 kd protein that contains a structural element homologous to the C2 region of protein kinase C.

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MSFIDPYQHI IVEHQYSHKF TVVVLRATKV TKGAFGDMLD TPDPYVELFI STTPDSRKRT    60
RHFNNDINPV WNETFEFILD PNQENVLEIT LMDANYVMDE TLGTATFTVS SMKVGEKKEV   120
PFIFNQVTEM VLEMSLEVCS CPDLRFSMAL CDQEKTFRQQ RKEHIRESMK KLLGPKNSEG   180
LHSARDVPVV AILGSGGGFR AMVGFSGVMK ALYESGILDC ATYVAGLSGS TWYMSTLYSH   240
PDFPEKGPEE INEELMKNVS HNPLLLLTPQ KVKRYVESLW KKKSSGQPVT FTDIFGMLIG   300
ETLIHNRMNT TLSSLKEKVN TAQCPLPLFT CLHVKPDVSE LMFADWVEFS PYEIGMAKYG   360
TFMAPDLFGS KFFMGTVVKK YEENPLHFLM GVWGSAFSIL FNRVLGVSGS QSRGSTMEEE   420
LENITTKHIV SNDSSDSDDE SHEPKGTENE DAGSDYQSDN QASWIHRMIM ALVSDSALFN   480
TREGRAGKVH NFMLGLNLNT SYPLSPLSDF ATQDSFDDDE LDAAVADPDE FERIYEPLDV   540
KSKKIHVVDS GLTFNLPYPL ILRPQRGVDL IISFDFSARP SDSSPPFKEL LLAEKWAKMN   600
KLPFPKIDPY VFDREGLKEC YVFKPKNPDM EKDCPTIIHF VLANINFRKY KAPGVPRETE   660
EEKEIADFDI FDDPESPFST FNFQYPNQAF KRLHDLMHFN TLNNIDVIKE AMVESIEYRR   720
QNPSRCSVSL SNVEARRFFN KEFLSKPKA
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ACA1 protein sequence
Gene name: tissue factor pathway inhibitor 2 TFPI2, placental protein 5 (PP5)
Unigene number: Hs.78045
Probeset Accession #: D29992
Protein Accession #: BAA06272.1
Pfam: Kunitz BPTI
Signal sequence: underlined
Summary: ACA1 is a serine proteinase inhibitor that was originally purified from conditioned medium of the human glioblastoma cell line T98G. ACA1 is identical to placental protein 5 (PP5) and TFPI2, a placenta-derived glycoprotein with serine proteinase inhibitor activity. PP5 belongs to the Kunitz-type serine proteinase inhibitor family, having three putative Kunitz-type inhibitor domains.

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MDPARPLGLS ILLLFLTEAA LGDAAQEPTG NNAEICLLPL DYGPCRALLL RYYYDRYTQS    60
CRQFLYGGCE GNANNFYTWE ACDDACWRIE KVPKVCRLQV SVDDQCEGST EKYFFNLSSM   120
TCEKFFSGGC HRNRIENRFP DEATCMGFCA PKKIPSFCYS PKDEGLCSAN VTRYYFNPRY   180
RTCDAFTYTG CGGNDNNFVS REDCKRACAK ALKKKKKMPK LRFASRIRKI RKKQF
```

ACB8 protein sequence
Gene name: myosin X
Unigene number: Hs.61638
Probeset Accession #: N77151
Protein Accession #: NP_036466
Pfam: myosin head, IQ (calmodulin binding motif), PH, MyTH4
Summary: Myosins are molecular motors that move along filamentous actin. Seven classes of myosin are expressed in vertebrates: conventional myosin, or myosin-II, as well as the 6 unconventional myosin classes-I, -V, -VI, -VII, -IX, and -X.

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MDNFFTEGTR VWLRENGQHF PSTVNSCAEG IVVFRTDYGQ VFTYKQSTIT HQKVTAMHPT    60
NEEGVDDMAS LTELHGGSIM YNLFQRYKRN QIYTYIGSIL ASVNPYQPIA GLYEPATMEQ   120
YSRRHLGELP PHIFAIANEC YRCLWKRYDN QCILISGESG AGKTESTKLI LKFLSVISQQ   180
SLELSLKEKT SCVERAILES SPIMEAFGNA KTVYNNNSSR FGKFVQLNIC QKGNIQGGRI   240
VDYLLEKNRV VRQNPGERNY HIFYALLAGL EHEEREEFYL STPENYHYLN QSGCVEDKTI   300
SDQESFREVI TAMDVMQFSK EEVREVSRLL AGILHLGNIE FITAGGAQVS FKTALGRSAE   360
LLGLDPTQLT DALTQRSMFL RGEEILTPLN VQQAVDSRDS LAMALYACCF EWVIKKINSR   420
IKGNEDFKSI GILDIFGFEN FEVNHFEQFN INYANEKLQE YFNKHIFSLE QLEYSREGLV   480
WEDIDWIDNG ECLDLIEKKL GLLALINEES HFPQATDSTL LEKLHSQHAN NHFYVKPRVA   540
VNNFGVKHYA GEVQYDVRGI LEKNRDTFRD DLLNLLRESR FDFIYDLFEH VSSRNNQDTL   600
KCGSKHRRPT VSSQFKDSLH SLMATLSSSN PFFVRCIKPN MQKMPDQFDQ AVVLNQLRYS   660
GMLETVRIRK AGYAVRRPFQ DFYKRYKVLM RNLALPEDVR GKCTSLLQLY DASNSEWQLG   720
KTKVFLRESL EQKLEKRREE EVSHAAMVIR AHVLGFLARK QYRKVLYCVV IIQKNYRAFL   780
LRRRFLHLKK AAIVFQKQLR GQIARRVYRQ LLAEKREQEE KKKQEEEEKK KREEEERERE   840
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RERREAELRA QQEEETRKQQ ELEALQKSQK EAELTRELEK QKENKQVEEI LRLEKEIEDL 900
QRMKEQQELS LTEASLQKLQ ERRDQELRRL EEEACRAAQE FLESLNFDEI DECVRNIERS 960
LSVGSEFSSE LAESACEEKP NFNFSQPYPE EEVDEGFEAD DDAFKDSPNP SEHGHSDQRT 1020
SGIRTSDDSS EEDPYMNDTV VPTSPSADST VLLAPSVQDS GSLHNSSSGE STYCMPQNAG 1080
DLPSPDGDYD YDQDDYEDGA ITSGSSVTFS NSYGSQWSPD YRCSVGTYNS SGAYRFSSEG 1140
AQSSFEDSEE DFDSRFDTDD ELSYRRDSVY SCVTLPYFHS FLYMKGGLMN SWKRRWCVLK 1200
DETFLWFRSK QEALKQGWLH KKGGGSSTLS RRNWKKRWFV LRQSKLMYFE NDSEEKLKGT 1260
VEVRTAKEII DNTTKENGID IIMADRTFHL IAESPEDASQ WFSVLSQVHA STDQEIQEMH 1320
DEQANPQNAV GTLDVGLIDS VCASDSPDRP NSFVIITANR VLHCNADTPE EMHHWITLLQ 1380
RSKGDTRVEG QEFIVRGWLH KEVKNSPKMS SLKLKKRWFV LTHNSLDYYK SSEKNALKLG 1440
TLVLNSLCSV VPPDEKIFKE TGYWNVTVYG RKHCYRLYTK LLNEATRWSS AIQNVTDTKA 1500
PIDTPTQQLI QDIKENCLNS DVVEQIYKRN PILRYTHHPL HSPLLPLPYG DINLNLLKDK 1560
GYTTLQDEAI KIFNSLQQLE SMSDPIPIIQ GILQTGHDLR PLRDELYCQL IKQTNKVPHP 1620
GSVGNLYSWQ ILTCLSCTFL PSRGILKYLK FHLKRIREQF PGTEMEKYAL FTYESLKKTK 1680
CREFVPSRDE IEALIHRQEM TSTVYCHGGG SCKITINSHT TAGEVVEKLI RGLAMEDSRN 1740
MFALFEYNGH VDKAIESRTV VADVLAKFEK LAATSEVGDL PWKFYFKLYC FLDTDNVPKD 1800
SVEFAFMFEQ AHEAVIHGHH PAPEENLQVL AALRLQYLQG DYTLHAAIPP LEEVYSLQRL 1860
KARISQSTKT FTPCERLEKR RTSFLEGTLR RSFRTGSVVR QKVEEEQMLD MWIKEEVSSA 1920
RASIIDKWRK FQGMNQEQAM AKYMALIKEW PGYGSTLFDV ECKEGGFPQE LWLGVSADAV 1980
SVYKRGEGRP LEVFQYEHIL SFGAPLANTY KIVVDERELL FETSEVVDVA KLMKAYISMI 2040
VKKRYSTTRS ASSQGSSR

ACC3 protein sequence
Gene name: calcitonin receptor-like (CALCRL)
Unigene number: Hs.152175
Probeset Accession #: L76380
Protein Accession #: NP_005786.1
Pfam: 7TM 2 (7 transmembrane receptor (Secretin family))
Transmembrane domains: predictions underlined
Signal sequence: first underlined region
Summary: Calcitonin gene-related peptide (CGRP) is a neuropeptide with diverse biological effects including potent vasodilator activity. The human CGRP1 receptor shares significant peptide sequence homology with the human calcitonin receptor, a member of the G-protein-coupled receptor superfamily. Stable expression in 293 (HEK 293) cells produces specific, high affinity binding sites for CGRP. Exposure of these cells to CGRP results in a 60-fold increase in cAMP production.

MEKKCTLYFL VLLPFFMILV TAELEESPED SIQLGVTRNK IMTAQYECYQ KIMQDPIQQA 60
EGVYCNRTWD GWLCWNDVAA GTESMQLCPD YFQDFDPSEK VTKICDQDGN WFRHPASNRT 120
WTNYTQCNVN THEKVKTALN LFYLTIIGHG LSIASLLISL GIFFYFKSLS CQRITLHKNL 180
FFSFVCNSVV TIIHLTAVAN NQALVATNPV SCKVSQFIHL YLMGCNYFWM LCEGIYLHTL 240
IVVAVFAEKQ HLMWYYFLGW GFPLIPACIH AIARSLYYND NCWISSDTHL LYIIHGPICA 300
ALLVNLFFLL NIVRVLITKL KVTHQAESNL YMKAVRATLI LVPLLGIEFV LIPWRPEGKI 360
AEEVYDYIMH ILMHFQGLLV STIFCFFNGE VQAILRRNWN QYKIQFGNSF SNSEALRSAS 420
YTVSTISDGP GYSHDCPSEH LNGKSIHDIE NVLLKPENLY N

ACC5 protein sequence
Gene name: Selectin E (endothelial adhesion molecule 1)
Unigene number: Hs.89546
Probeset Accession #: M24736
Protein Accession #: NP_000441.1
Pfam: lectin c, EGF like domain, sushi (SCR domain)
Signal sequence: first underlined region
Transmembrane domain: second underlined region
Summary: Focal adhesion of leukocytes to the blood vessel lining is a key step in inflammation and certain vascular disease processes. Endothelial leukocyte adhesion molecule-1 (ELAM-1), a cell surface glycoprotein expressed by cytokine-activated endothelium, mediates the adhesion of blood neutrophils. The primary sequence of ELAM-1 predicts an amino-terminal lectin-like domain, an EGF domain, and six tandem repetitive motifs (about 60 amino acids each) related to those found in complement regulatory proteins. A similar domain structure is also found in the MEL-14 lymphocyte cell surface homing receptor, and in granule-membrane protein 140, a membrane glycoprotein of platelet and endothelial secretory granules that can be rapidly mobilized (less than 5 minutes) to the cell surface by thrombin and other stimuli. Thus, ELAM-1 may be a member of a nascent gene family of cell

surface molecules involved in the regulation of inflammatory and immunological events at the interface of vessel wall and blood.

MIASQFLSAL TLVLLIKESG AWSYNTSTEA MTYDEASAYC QQRYTHLVAI QNKEEIEYLN 60
SILSYSPSYY WIGIRKVNNV WVWVGTQKPL TEEAKNWAPG EPNNRQKDED CVEIYIKREK 120
DVGMWNDERC SKKKLALCYT AACTNTSCSG HGECVETINN YTCKCDPGFS GLKCEQIVNC 180
TALESPEHGS LVCSHPLGNF SYNSSCSISC DRGYLPSSME TMQCMSSGEW SAPIPACNVV 240
ECDAVTNPAN GFVECFQNPG SFPWNTTCTF DCEEGFELMG AQSLQCTSSG NWDNEKPTCK 300
AVTCRAVRQP QNGSVRCSHS PAGEFTFKSS CNFTCEEGFM LQGPAQVECT TQGQWTQQIP 360
VCEAFQCTAL SNPERGYMNC LPSASGSFRY GSSCEFSCEQ GFVLKGSKRL QCGPTGEWDN 420
EKPTCEAVRC DAVHQPPKGL VRCAHSPIGE FTYKSSCAFS CEEGFELYGS TQLECTSQGQ 480
WTEEVPSCQV VKCSSLAVPG KINMSCSGEP VFGTVCKFAC PEGWTLNGSA ARTCGATGHW 540
SGLLPTCEAP TESNIPLVAG LSAAGLSLLT LAPFLLWLRK CLRKAKKFVP ASSCQSLESD 600
GSYQKPSYIL

ACC8 protein sequence
Gene name: Chemokine (C-X-C motif), receptor 4 (fusin)
Unigene number: Hs.89414
Probeset Accession #: L06797
Protein Accession #: NP_003458.1
Pfam: 7TM_1 (7 transmembrane receptor (rhodopsin family))
Signal sequence: none identified
Transmembrane domains: predictions underlined
Summary: The chemokine receptor CXCR4 (also designated fusin and D2STR) is a cofactor for fusion and entry of T cell-tropic strains of HIV-1.

MEGISIYTSD NYTEEMGSGD YDSMKEPCFR EENANFNKIF LPTIYSIIFL TGIVGNGLVI 60
LVMGYQKKLR SMTDKYRLHL SVADLLFVIT LPFWAVDAVA NWYFGNFLCK AVHVIYTVNL 120
YSSVLILAFI SLDRYLAIVH ATNSQRPRKL LAEKVVYVGV WIPALLLTIP DFIFANVSEA 180
DDRYICDRFY PNDLWVVVFQ FQHIMVGLIL PGIVILSCYC IIISKLSHSK GHQKRKALKT 240
TVILILAFFA CWLPYYIGIS IDSFILLEII KQGCEFENTV HKWISITEAL AFFHCCLNPI 300
LYAFLGAKFK TSAQHALTSV SRGSSLKILS KGKRGGHSSV STESESSSFH SS

ACF2 protein sequence
Gene name: Endothelial cell-specific molecule 1
Unigene number: Hs.41716
Probeset Accession #: X89426
Protein Accession #: NP_008967.1
Signal sequence: underlined
Pfam: IGFBP (Insulin-like growth factor binding proteins)
Summary: Human endothelial cell-specific molecule (called ESM-1) was cloned from a human umbilical vein endothelial cell (HUVEC) cDNA library. Constitutive ESM-1 gene expression is seen in HUVECs but not in the other human cell lines. The cDNA sequence contains an open reading frame of 552 nucleotides and a 1398-nucleotide 3'-untranslated region including several domains involved in mRNA instability and five putative polyadenylation consensus sequences. The deduced 184-amino acid sequence defines a cysteine-rich protein with a functional NH2-terminal hydrophobic signal sequence.

MKSVLLLTTL LVPAHLVAAW SNNYAVDCPQ HCDSSECKSS PRCKRTVLDD CGCCRVCAAG 60
RGETCYRTVS GMDGMKCGPG LRCQPSNGED PFGEEFGICK DCPYGTFGMD CRETCNCQSG 120
ICDRGTGKCL KFPFFQYSVT KSSNRFVSLT EHDMASGDGN IVREEVVKEN AAGSPVMRKW 180
LNPR

ACF4 protein sequence
Gene name: P53-responsive gene 2 similar to D.melanogaster peroxidasin(U11052)
Unigene number: Hs.118893
Probeset Accession #: D86983
Protein Accession #: BAA13219
Pfam: LRRNT (Leucine rich repeat N-terminal domain), LRR (Leucine Rich Repeat), LRRCT (Leucine rich repeat C-terminal domain), Ig (immunoglobulin domain), Peroxidase, VWC (von Willebrand factor type C domain)
Summary: ACF4 is a gene originally identified from KG-1 cell and brain cDNA libraries.

SRPWWLRASE RPSAPSAMAK RSRGPGRRCL LALVLFCAWG TLAVVAQKPG AGCPSRCLCF 60
RTTVRCMHLL LEAVPAVAPQ TSILDLRFNR IREIQPGAFR RLRNLNTLLL NNNQIKRIPS 120
GAFEDLENLK YLYLYKNEIQ SIDRQAFKGL ASLEQLYLHF NQIETLDPDS FQHLPKLERL 180
FLHNNRITHL VPGTFNHLES MKRLRLDSNT LHCDCEILWL ADLLKTYAES GNAQAAAICE 240
YPRRIQGRSV ATITPEELNC ERPRITSEPQ DADVTSGNTV YFTCRAEGNP KPEIIWLRNN 300
NELSMKTDSR LNLLDDGTLM IQNTQETDQG IYQCMAKNVA GEVKTQEVTL RYFGSPARPT 360
FVIQPQNTEV LVGESVTLEC SATGHPPPRI SWTRGDRTPL PVDPRVNITP SGGLYIQNVV 420
QGDSGEYACS ATNNIDSVHA TAFIIVQALP QFTVTPQDRV VIEGQTVDFQ CEAKGNPPPV 480
IAWTKGGSQL SVDRRHLVLS SGTLRISGVA LHDQGQYECQ AVNIIGSQKV VAHLTVQPRV 540
TPVFASIPSD TTVEVGANVQ LPCSSQGEPE PAITWNKDGV QVTESGKFHI SPEGFLTIND 600
VGPADAGRYE CVARNTIGSA SVSMVLSVNV PDVSRNGDPF VATSIVEAIA TVDRAINSTR 660
THLFDSRPRS PNDLLALFRY PRDPYTVEQA RAGEIFERTL QLIQEHVQHG LMVDLNGTSY 720
HYNDLVSPQY LNLIANLSGC TAHRRVNNCS DMCFHQKYRT HDGTCNNLQH PMWGASLTAF 780
ERLLKSVYEN GFNTPRGINP HRLYNGHALP MPRLVSTTLI GTETVTPDEQ FTHMLMQWGQ 840
FLDHDLDSTV VALSQARFSD GQHCSNVCSN DPPCFSVMIP PNDSRARSGA RCMFFVRSSP 900
VCGSGMTSLL MNSVYPREQI NQLTSYIDAS NVYGSTEHEA RSIRDLASHR GLLRQGIVQR 960
SGKPLLPFAT GPPTECMRDE NESPIPCFLA GDHRANEQLG LTSMHTLWFR EHNRIATELL 1020
KLNPHWDGDT IYYETRKIVG AEIQHITYQH WLPKILGEVG MRTLGEYHGY DPGINAGIFN 1080
AFATAAFRFG HTLVNPLLYR LDENFQPIAQ DHLPLHKAFF SPFRIVNEGG IDPLLRGLFG 1140
VAGKMRVPSQ LLNTELTERL FSMAHTVALD LAAINIQRGR DHGIPPYHDY RVYCNLSAAH 1200
TFEDLKNEIK NPEIREKLKR LYGSTLNIDL FPALVVEDLV PGSRLGPTLM CLLSTQFKRL 1260
RDGDRLWYEN PGVFSPAQLT QIKQTSLARI LCDNADNITR VQSDVFRVAE FPHGYGSCDE 1320
IPRVDLRVWQ DCCEDCRTRG QFNAFSYHFR GRRSLEFSYQ EDKPTKKTRP RKIPSVGRQG 1380
EHLSNSTSAF STRSDASGTN DFREFVLEMQ KTITDLRTQI KKLESRLSTT ECVDAGGESH 1440
ANNTKWKKDA CTICECKDGQ VTCFVEACPP ATCAVPVNIP GACCPVCLQK RAEEKP

ACF5 protein sequence
Gene name: Mitogen-activated protein kinase kinase kinase kinase 4
Unigene number: Hs.3628
Probeset Accession #: N54067
Protein Accession #: NP_004825.1
Pfam: pkinase (Eukaryotic protein kinase domain), CNH domain
Summary: The yeast serine/threonine kinase STE20 activates a signaling cascade that includes STE11 (mitogen-activated protein kinase kinase kinase), STE7 (mitogen-activated protein kinase kinase), and FUS3/KSS1 (mitogen-activated protein kinase) in response to signals from both Cdc42 and the heterotrimeric G proteins associated with transmembrane pheromone receptors. ACF5 is a human cDNA encoding a protein kinase homologous to STE20. This protein kinase, also designated HPK/GCK-like kinase (HGK), has nucleotide sequences that encode an open reading frame of 1165 amino acids with 11 kinase subdomains. HGK is a serine/threonine protein kinase that specifically activated the c-Jun N-terminal kinase (JNK) signaling pathway when transfected into 293T cells, but does not stimulate either the extracellular signal-regulated kinase or p38 kinase pathway. HGK also increased AP-1-mediated transcriptional activity in vivo. HGK may be a novel activator of the JNK pathway. The cascade may look like this:HGK -> TAK1 -> MKK4, MKK7 -> JNK kinase cascade, which may mediate the TNF-alpha signaling pathway.

MANDSPAKSL VDIDLSSLRD PAGIFELVEV VGNGTYGQVY KGRHVKTGQL AAIKVMDVTE 60
DEEEEIKLEI NMLKKYSHHR NIATYYGAFI KKSPPGHDDQ LWLVMEFCGA GSITDLVKNT 120
KGNTLKEDWI AYISREILRG LAHLHIHHVI HRDIKGQNVL LTENAEVKLV DFGVSAQLDR 180
TVGRRNTFIG TPYWMAPEVI ACDENPDATY DYRSDLWSCG ITAIEMAEGA PPLCDMHPMR 240
ALFLIPRNPP PRLKSKKWSK KFFSFIEGCL VKNYMQRPST EQLLKHPFIR DQPNERQVRI 300
QLKDHIDRTR KKRGEKDETE YEYSGSEEEE EEVPEQEGEP SSIVNVPGES TLRRDFLRLQ 360
QENKERSEAL RRQQLLQEQQ LREQEEYKRQ LLAERQKRIE QQKEQRRRLE EQQRREREAR 420
RQQEREQRRR EQEEKRRLEE LERRRKEEEE RRRAEEEKRR VEREQEYIRR QLEEEQRHLE 480
VLQQQLLQEQ AMLLHDHRRP HPQHSQQPPP PQQERSKPSF HAPEPKAHYE PADRAREVPV 540
RTTSRSPVLS RRDSPLQGSG QQNSQAGQRN STSIEPRLLW ERVEKLVPRP GSGSSSGSSN 600
SGSQPGSHPG SQSGSGERFR VRSSSKSEGS PSQRLENAVK KPEDKKEVFR PLKPAGEV[illegible] 660
TALAKELRAV EDVRPPHKVT DYSSSSEESG TTDEEDDDVE QEGADESTSG PEDTRAAS[illegible] 720
NLSNGETESV KTMIVHDDVE SEPAMTPSKE GTLIVRQTQS ASSTLQKHKS SSSFTPFIDP 780
RLLQISPSSG TTVTSVVGFS CDGMRPEAIR QDPTRKGSVV NVNPTNTRPQ SDTPEIRKYK 840
KRFNSEILCA ALWGVNLLVG TESGLMLLDR SGQGKVYPLI NRRRFQQMDV LEGLNVLVTI 900
SGKKDKLRVY YLSWLRNKIL HNDPEVEKKQ GWTTVGDLEG CVHYKVVKYE RIKFLVIALK 960
SSVEVYAWAP KPYHKFMAFK SFGELVHKPL LVDLTVEEGQ RLKVIYGSCA GFHAVDVDSG 1020
SVYDIYLPTH VRKNPHSMIQ CSIKPHAIII LPNTDGMELL VCYEDEGVYV NTYGRITKDV 1080
VLQWGEMPTS VAYIRSNQTM GWGEKAIEIR SVETGHLDGV FMHKRAQRLK FLCERNDKVF 1140

FASVRSGGSS QVYFMTLGRT SLLSW

ACF8 protein sequence
Gene name: Phospholipase A2, group IVC (cytosolic, calcium-independent)
Unigene number: Hs.18858
Probeset Accession #: AA054087
Protein Accession #: NP_003697.1
Pfam: none identified
Summary: ACF8 is a membrane-bound, calcium-independent PLA2 named cPLA2-gamma. The sequence encodes a 541-amino acid protein containing a domain with significant homology to the catalytic domain of the 85-kDa cPLA2 (cPLA2-alpha). cPLA2-gamma does not contain the regulatory calcium-dependent lipid binding (CaLB) domain found in cPLA2-alpha. cPLA2-gamma does contain two consensus motifs for lipid modification, a prenylation motif (-CCLA) at the C terminus and a myristoylation site at the N terminus. cPLA2-gamma demonstrates a preference for arachidonic acid at the sn-2 position of phosphatidylcholine as compared with palmitic acid. cPLA2-gamma encodes a 3-kilobase message, which is highly expressed in heart and skeletal muscle, suggesting a specific role in these tissues.

MGSSEVSIIP GLQKEEKAAV ERRRLHVLKA LKKLRIEADE APVVAVLGSG GGLRAHIACL 60
GVLSEMKEQG LLDAVTYLAG VSGSTWAISS LYTNDGDMEA LEADLKHRFT RQEWDLAKSL 120
QKTIQAARSE NYSLTDFWAY MVISKQTREL PESHLSNMKK PVEEGTLPYP IFAAIDNDLQ 180
PSWQEARAPE TWFEFTPHHA GFSALGAFVS ITHFGSKFKK GRLVRTHPER DLTFLRGLWG 240
SALGNTEVIR EYIFDQLRNL TLKGLWRRAV ANAKSIGHLI FARLLRLQES SQGEHPPPED 300
EGGEPEHTWL TEMLENWTRT SLEKQEQPHE DPERKGSLSN LMDFVKKTGI CASKWEWGTT 360
HNFLYKHGGI RDKIMSSRKH LHLVDAGLAI NTPFPLVLPP TREVHLILSF DFSAGDPFET 420
IRATTDYCRR HKIPFPQVEE AELDLWSKAP ASCYILKGET GPVVIHFPLF NIDACGGDIE 480
AWSDTYDTFK LADTYTLDVV VLLLALAKKN VRENKKKILR ELMNVAGLYY PKDSARSCCL 540
A

ACG1 protein sequence
Gene name: Carbohydrate (chondroitin 6/keratan) sulfotransferase 1
Unigene number: Hs.104576
Probeset Accession #: AA868063
Protein Accession #: NP_003645.1
Pfam: none identified
Summary: Chondroitin 6-sulfotransferase (C6ST) is the key enzyme in the biosynthesis of chondroitin 6-sulfate, a glycosaminoglycan implicated in chondrogenesis, neoplasia, atherosclerosis, and other processes. C6ST catalyzes the transfer of sulfate from 3'-phosphoadenosine 5'-phosphosulfate to carbon 6 of the N-acetylgalactosamine residues of chondroitin.

MQCSWKAVLL LALASIAIQN TAIRTFTAKS FHTCPGLAEA GLAERLCEES PTFAYNLSRK 60
THILILATTR SGSSFVGQLF NQHLDVFYLF EPLYHVQNTL IPRFTQGKSP ADRRVMLGAS 120
RDLLRSLYDC DLYFLENYIK PPPVNHTTDR IFRRGASRVL CSRPVCDPPG PADLVLEEGD 180
CVRKCGLLNL TVAAEACRER SHVAIKTVRV PEVNDLRALV EDPRLNLKVI QLVRDPRGIL 240
ASRSETFRDT YRLWRLWYGT GRKPYNLDVT QLTTVCEDFS NSVSTGLMRP PWLKGKYMLV 300
RYEDLARNPM KKTEEIYGFL GIPLDSHVAR WIQNNTRGDP TLGKHKYGTV RNSAATAEKW 360
RFRLSYDIVA FAQNACQQVL AQLGYKIAAS EEELKNPSVS LVEERDFRPF S

ACG5 protein sequence
Gene name: Multimerin
Unigene number: Hs.268107
Probeset Accession #: U27109
Protein Accession #: AAC52065
Sign : sequence: prediction underlined
Pfam. EGF-like domain, C1q domain
Summary: Multimerin is a massive, soluble protein found in platelets and in the endothelium of blood vessels. Multimerin is composed of varying sized, disulfide-linked multimers, the smallest of which is a homotrimer. Multimerin is a factor V/Va-binding protein and may function as a carrier protein for platelet factor V. Northern analyses show a 4.7-kilobase transcript in cultured endothelial cells, a megakaryocytic cell line, platelets, and highly vascular tissues. The multimerin cDNA can encode a protein of 1228 amino acids with the probable signal peptide

cleavage site between amino acids 19 and 20. The protein is predicted to be hydrophilic and to contain 23 N-glycosylation sites. The adhesive motif RGDS (Arg-Gly-Asp-Ser) and an epidermal growth factor-like domain were identified. Multimerin contains a probable coiled-coil structures in the central portion of its sequence. Additionally, the carboxyl-terminal region of multimerin resembles the globular, non-collagen-like, carboxyl-terminal domains of several other trimeric proteins, including complement C1q and collagens type VIII and X.

MKGARLFVLL SSLWSGGIGL NNSKHSWTIP EDGNSQKTMP SASVPPNKIQ SLQILPTTRV 60
MSAEIATTPE ARTSEDSLLK STLPPSETSA PAEGVRNQTL TSTEKAEGVV KLQNLTLPTN 120
ASIKFNPGAE SVVLSNSTLK FLQSFARKSN EQATSLNTVG GTGGIGGVGG TGGVGNRAPR 180
ETYLSRGDSS SSQRTDYQKS NFETTRGKNW CAYVHTRLSP TVTLDNQVTY VPGGKGPCGW 240
TGGSCPQRSQ KISNPVYRMQ HKIVTSLDWR CCPGYSGPKC QLRAQEQQSL IHTNQAESHT 300
AVGRGVAEQQ QQQGCGDPEV MQKMTDQVNY QAMKLTLLQK KIDNISLTVN DVRNTYSSLE 360
GKVSEDKSRE FQSLLKGLKS KSINVLIRDI VREQFKIFQN DMQETVAQLF KTVSSLSEDL 420
ESTRQIIQKV NESVVSIAAQ QKFVLVQENR PTLTDIVELR NHIVNVRQEM TLTCEKPIKE 480
LEVKQTHLEG ALEQEHSRSI LYYESLNKTL SKLKEVHEQL LSTEQVSDQK NAPAAESVSN 540
NVTEYMSTLH ENIKKQSLMM LQMFEDLHIQ ESKINNLTVS LEMEKESLRG ECEDMLSKCR 600
NDFKFQLKDT EENLHVLNQT LAEVLFPMDN KMDKMSEQLN DLTYDMEILQ PLLEQGASLR 660
QTMTYEQPKE AIVIRKKIEN LTSAVNSLNF IIKELTKRHN LLRNEVQGRD DALERRINEY 720
ALEMEDGLNK TMTIINNAID FIQDNYALKE TLSTIKDNSE IHHKCTSDME TILTFIPQFH 780
RLNDSIQTLV NDNQRYNFVL QVAKTLAGIP RDEKLNQSNF QKMYQMFNET TSQVRKYQQN 840
MSHLEEKLLL TTKISKNFET RLQDIESKVT QTLIPYYISV KKGSVVTNER DQALQLQVLN 900
SRFKALEAKS IHLSINFFSL NKTLHEVLTM CHNASTSVSE LNATIPKWIK HSLPDIQLLQ 960
KGLTEFVEPI IQIKTQAALS NSTCCIDRSL PGSLANVVKS QKQVKSLPKK INALKKPTVN 1020
LTTVLIGRTQ RNTDNIIYPE EYSSCSRHPC QNGGTCINGR TSFTCACRHP FTGDNCTIKL 1080
VEENALAPDF SKGSYRYAPM VAFFASHTYG MTIPGPILFN NLDVNYGASY TPRTGKFRIP 1140
YLGVYVFKYT IESFSAHISG FLVVDGIDKL AFESENINSE IHCDRVLTGD ALLELNYGQE 1200
VWLRLAKGTI PAKFPPVTTF SGYLLYRT

ACC6 protein sequence
Gene name: Homo sapiens cDNA FLJ11502 fis, clone HEMBA1002102, weakly similar to ANKRYIN
Unigene number: Hs.213194
Probeset Accession #: AA187101
Protein Accession #: none
Pfam: ankyrin repeats

VAARPPVSRM EPRAADGCFL GDVGFWVERT PVHEAAQRGE SLQLQQLIES GACVNQVTVD 60
SITPLHAASL QGQARCVQLL LAAGAQVDAR NIDGSTPLCD ACASGSIECV KLLLSYGAKV 120
NPPLYTASPL HEASFPRLLS TLASTPWIN

ACC7 protein sequence
Gene name: Human RAL A gene
Unigene number: Hs.6906
Probeset Accession #: AA083572 cluster
Protein Accession #: P11233
Pfam: ras
Features: CAAX motif is underlined
Summary: The RALA gene encodes a low molecular mass ras-like GTP-binding protein that shares about 50% similarity with the ras proteins. GTP-binding proteins mediate the transmembrane signaling initiated by the occupancy of certain cell surface receptors. The RALA gene maps to 7p22-p15.

MAANKPKGQN SLALHKVIMV GSGGVGKSAL TLQFMYDEFV EDYEPTKADS YRKKVVLDGE 60
EVQIDILDTA GQEDYAAIRD NYFRSGEGFL CVFSITEMES FAATADFREQ ILRVKEDENV 120
PFLLVGNKSD LEDKRQVSVE EAKNRAEQWN VNYVETSAKT RANVDKVFFD LMREIRARKM 180
EDSKEKNGKK KRKSLAKRIR ERCC

ACC9 protein sequence
Gene name: KIAA0985 protein
Unigene number: Hs.10031
Probeset Accession #: AA027168
Protein Accession #: BAA76799.1
Pfam: CARD (Caspase recruitment domain)

Summary: Gene was originally isolated as a brain cDNA. The coding region contains a CARD domain, suggesting involvement in apoptotic signaling pathways.

MMRQRQSHYC SVLFLSVNYL GGTFPGDICS EENQIVSSYA SKVCFEIEED YKNRQFLGPE 60
GNVDVELIDK STNRYSVWFP TAGWYLWSAT GLGFLVRDEV TVTIAFGSWS QHLALDLQHH 120
EQWLVGGPLF DVTAEPEEAV AEIHLPHFIS LQGEVDVSWF LVAHFKNEGM VLEHPARVEP 180
FYAVLESPSF SLMGILLRIA SGTRLSIPIT SNTLIYYHPH PEDIKFHLYL VPSDALLTKA 240
IDDEEDRFHG VRLQTSPPME PLNFGSSYIV SNSANLKVMP KELKLSYRSP GEIQHFSKFY 300
AGQMKEPIQL EITEKRHGTL VWDTEVKPVD LQLVAASAPP PFSGAAFVKE NHRQLQARMG 360
DLKGVLDDLQ DNEVLTENEK ELVEQEKTRQ SKNEALLSMV EKKGDLALDV LFRSISERDP 420
YLVSYLRQQN L

ACF6 Protein sequence

Gene name: Homo sapiens cDNA FLJ10669 fis, clone NT2RP2006275, weakly similar to Microtubule-associated protein 1B [CONTAINS: LIGHT CHAIN LC1]
Unigene number: Hs.66048
Probeset Accession #: AA609717
Protein Accession #: BAA91743.1
Pfam: none identified
Summary: The cDNA for FLJ10669 was originally isolated from NT2 neuronal precursor cells (teratocarcinoma cell line) after 2-weeks of retinoic acid (RA) treatment. The protein sequence has similarity to microtubule-associated protein 1B (MAP-1B), suggesting a function for ACF6 in the regulating the cytoskeleton.

MGVGRLDMYV LHPPSAGAER TLASVCALLV WHPAGPGEKV VRVLFPGCTP PACLLDGLVR 60
LQHLRFLREP VVTPQDLEGP GRAESKESVG SRDSSKREGL LATHPRPGQE RPGVARKEPA 120
RAEAPRKTEK EAKTPRELKK DPKPSVSRTQ PREVRRAASS VPNLKKTNAQ AAPKPRKAPS 180
TSHSGFPPVA NGPRSPPSLR CGEASPPSAA CGSPASQLVA TPSLELGPIP AGEEKALELP 240
LAASSIPRPR TPSPESHRSP AEGSERLSLS PLRGGEAGPD ASPTVTTPTV TTPSLPAEVG 300
SPHSTEVDES LSVSFEQVLP PSAPTSEAGL SLPLRGPRAR RSASPHDVDL CLVSPCEFEH 360
RKAVPMAPAP ASPGSSNDSS ARSQERAGGL GAEETPPTSV SESLPTLSDS DPVPLAPGAA 420
DSDEDTEGFG VPRHDPLPDP LKVPPPLPDP SSICMVDPEM LPPKTARQTE NVSRTRKPLA 480
RPNSRAAAPK ATPVAAAKTK GLAGGDRASR PLSARSEPSE KGGRAPLSRK SSTPKTATRG 540
PSGSASSRPG VSATPPKSPV YLDLAYLPSG SSAHLVDEEF FQRVRALCYV ISGQDQRKEE 600
GMRAVLDALL ASKQHWDRDL QVTLIPTFDS VAMHTWYAET HARHQALGIT VLGSNGMVSM 660
QDDAFPACKV EF